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cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy) blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious bliseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications include indications include
cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditic such as, for example, hyperplasia, metaplasia, and/or dysplasia.	7 8 0 1 0 1 0 3 1 0 0
Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin production. The DMEF1 response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive glucose transporter in fat and muscle tissue. Exemplary assays that may be used or routinely modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed inThai, M.V., et al., J Biol Chem,
	Regulation of transcription via DMEF1 response element in adipocytes and pre-adipocytes
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	HNGDX18
	595

				273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-21 (1994); "Identification of a 30-base pair regulatory element and novel DNA binding protein that regulates the human GLUT4 promoter in transgenic mice", J Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L cell line	weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
295	HNGDX18	800	Activation of transcription through GAS response element in immune cells (such as T-cells).	which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adiposelike conversion under appropriate differentiation culture conditions. Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or

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			transcription through the GAS response	dysnlasia Preferred indications include autoimmune
			element that may be used or routinely	oi.
			modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
			activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
			(including antibodies and agonists or	boosting a T cell-mediated immune response, and
			antagonists of the invention) include	suppressing a T cell-mediated immune response.
			assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
			66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
			Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
			Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
			85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
			Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
			Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
			4587 (1995), the contents of each of which	and/or an infectious disease as described below under
			are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
			entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
			may be used according to these assays are	ö
			publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
			ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS
			used according to these assays include the	granulomatous disease, inflammatory bowel disease,
			CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
			culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues.
			cells.	hemophilia hypercoagulation diabetes mellitus
				proceeditis maninatis I am Disease and authority
				allergy.
295 HNGDX18	608	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
		transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
		serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
		in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
		as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
-			(including antibodies and agonists or	include blood disorders (e.g., as described below under
			antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
			the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
			the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
			growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
			transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
			used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated

				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
	· · · · · · · · · · · · · · · · · · ·			incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
,				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
700	INCORYA	0.50	- 1	and the second s	under "Intectious Disease").
720	FINGUI 34	018	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliterative diseases.	Activity", "Blood-Related Disorders", and/or

	Account for imminomodulatory and	"Cooperation Discontinual of the state of th
	differentiation factor proteins produced by	described below under "Infactions Disease") Highly
	a large variety of cells where the	preferred indications include autoimmune diseases (e.g.
	expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis.
	cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
	are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
	or routinely modified to assess the ability	preferred indications also include boosting a B cell-
	of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
	antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
	the invention) to mediate	indications include inflammation and inflammatory
-	immunomodulation and differentiation and	disorders. Additional highly preferred indications include
	modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
	Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
	immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
	production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
	the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
	proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
	Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
-	modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
	diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
	the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
	agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
	include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
	J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
	204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
	a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
	(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
	158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
	each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
	reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
	cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
	assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
	disclosed herein or otherwise known in the	described below under "Infectious Disease").
	art. Human dendritic cells are antigen	
	presenting cells in suspension culture,	
-	which, when activated by antigen and/or	
	cytokines, initiate and upregulate T cell	

				nroliforation and functional activities	
707	UNICEASA	011	- 1	Figure and functional activities.	
167	nivoeA34	110	Production of IL-5	L-5 FMAT. Assays for	A highly preferred embodiment of the invention
		-		immunomodulatory proteins secreted by	includes a method for inhibiting (e.g., reducing) IL-5
				TH2 cells, mast cells, basophils, and	production. An alternative highly preferred embodiment of
				eosinophils that stimulate eosinophil	the invention includes a method for stimulating (e.g.,
				function and B cell Ig production and	increasing) IL-5 production. A highly preferred
				promote polarization of CD4+ cells into	embodiment of the invention includes a method for
				TH2 cells are well known in the art and	stimulating (e.g., increasing) immunoglobulin production.
				may be used or routinely modified to	An alternative highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for inhibiting (e.g.,
				invention (including antibodies and	decreasing) immunoglobulin production. A highly
				agonists or antagonists of the invention) to	7
				mediate immunomodulation, stimulate	
				immune cell function, modulate B cell Ig	
				production, modulate immune cell	highly preferred indication is infection (e.g., an infectious
				polarization, and/or mediate humoral or	disease as described below under "Infectious Disease"),
				cell-mediated immunity. Exemplary	and inflammation and inflammatory disorders.
				assays that test for immunomodulatory	Preferred indications include blood disorders (e.g., as
				proteins evaluate the production of	described below under "Immune Activity", "Blood-
				cytokines, such as IL-5, and the	Related Disorders", and/or "Cardiovascular Disorders").
				stimulation of eosinophil function and B	Preferred indications include autoimmune diseases (e.g.,
				cell Ig production. Such assays that may	rheumatoid arthritis, systemic lupus erythematosis,
-				be used or routinely modified to test	multiple sclerosis and/or as described below) and
				immunomodulatory activity of	immunodeficiencies (e.g., as described below).
				polypeptides of the invention (including	Preferred indications include neoplastic diseases (e.g.,
				antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and/or as described
				the invention) include the assays disclosed	below under "Hyperproliferative Disorders"), Preferred
				in Miraglia et al., J Biomolecular	indications include neoplasms and cancers, such as,
				Screening 4:193-204 (1999); Rowland et	leukemia, lymphoma, melanoma, and prostate, breast,
				al., "Lymphocytes: a practical approach"	lung, colon, pancreatic, esophageal, stomach, brain, liver
				Chapter 6:138-160 (2000); Ohshima et al.,	and urinary cancer. Other preferred indications include
-				Blood 92(9):3338-3345 (1998); Jung et al.,	benign dysproliferative disorders and pre-neoplastic
				Eur J Immunol 25(8):2413-2416 (1995);	conditions, such as, for example, hyperplasia, metaplasia,
				Mori et al., J Allergy Clin Immunol 106(1	and/or dysplasia. Preferred indications include anemia,
				Pt 2):558-564 (2000); and Koning et al.,	pancytopenia, leukopenia, thrombocytopenia, leukemias,
				Cytokine 9(6):427-436 (1997), the	Hodgkin's disease, acute lymphocytic anemia (ALL),
				contents of each of which are herein	plasmacytomas, multiple myeloma, Burkitt's lymphoma,

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·				incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
298	HNGEQ75	812	Protection from Endothelial Cell Apoptosis.	Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to inhibit caspase proteasemediated apoptosis. Exemplary assays for caspase apoptosis that may be used or routinely modified to test caspase apoptosis rescue of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Romeo et al., Cardiovasc Res 45(3): 788-794 (2000); Messmer et al., Br J Pharmacol 127(7): 1633-1640 (1999); and J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating angiogenisis. An alternative highly preferred
				that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary endothelial cells that may be used according to these assays include bovine	embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method

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		aortic endothelial cells (bAEC), which are	for inducing cardiac hypertrophy. Highly preferred
		an example of endothelial cells which line blood vessels and are involved in functions	indications include neoplastic diseases (e.g., as described
		that include but are not limited to	disorders of the cardiovascular system (a g. bour disease
		angiogenesis, vascular nermeahility	congestive heart failure hypertension acutic stenosis
		vascular tone, and immune cell	cardiomyopathy, valvular regurgitation, left ventricular
		extravasation.	dysfunction, atherosclerosis and atherosclerotic vascular
			disease, diabetic nephropathy, intracardiac shunt, cardiac
			hypertrophy, myocardial infarction, chronic hemodynamic
			overload, and/or as described below under
			"Cardiovascular Disorders"). Highly preferred
			indications include cardiovascular, endothelial and/or
			angiogenic disorders (e.g., systemic disorders that affect
			vessels such as diabetes mellitus, as well as diseases of the
			vessels themselves, such as of the arteries, capillaries,
			veins and/or lymphatics). Highly preferred are indications
	_		that stimulate angiogenesis and/or cardiovascularization.
	•		Highly preferred are indications that inhibit angiogenesis
			and/or cardiovascularization. Highly preferred
			indications include antiangiogenic activity to treat solid
			tumors, leukemias, and Kaposi's sarcoma, and retinal
			disorders. Highly preferred indications include neoplasms
			and cancer, such as, Kaposi's sarcoma, hemangioma
			(capillary and cavernous), glomus tumors, telangiectasia,
			bacillary angiomatosis, hemangioendothelioma,
1.			angiosarcoma, haemangiopericytoma, lymphangioma,
			lymphangiosarcoma. Highly preferred indications also
			include cancers such as, prostate, breast, lung, colon,
			pancreatic, esophageal, stomach, brain, liver, and urinary
			cancer. Preferred indications include benign
			dysproliferative disorders and pre-neoplastic conditions,
			such as, for example, hyperplasia, metaplasia, and/or
			dysplasia. Highly preferred indications also include
			arterial disease, such as, atherosclerosis, hypertension,
			coronary artery disease, inflammatory vasculitides,
			Reynaud's disease and Reynaud's phenomenom,
			aneurysms, restenosis; venous and lymphatic disorders

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					such as thrombophlebitis, lymphangitis, and lymphedema;
		-			9
					disease, and cancer. Highly preferred indications also
					include trauma such as wounds, burns, and injured tissue
					(e.g., vascular injury such as, injury resulting from balloon
					angioplasty, and atheroschlerotic lesions), implant
					fixation, scarring, ischemia reperfusion injury, rheumatoid
					둳
					acute renal failure, and osteoporosis. Additional highly
					preferred indications include stroke, graft rejection,
					diabetic or other retinopathies, thrombotic and coagulative
					disorders, vascularitis, lymph angiogenesis, sexual
					disorders, age-related macular degeneration, and treatment
					/prevention of endometriosis and related conditions.
					Additional highly preferred indications include fibromas,
					heart disease, cardiac arrest, heart valve disease, and
					vascular disease. Preferred indications include blood
					disorders (e.g., as described below under "Immune
					Activity", "Blood-Related Disorders", and/or
					"Cardiovascular Disorders"). Preferred indications include
					autoimmune diseases (e.g., rheumatoid arthritis, systemic
					lupus erythematosis, multiple sclerosis and/or as described
					below) and immunodeficiencies (e.g., as described below).
					Additional preferred indications include inflammation and
					inflammatory disorders (such as acute and chronic
					inflammatory diseases, e.g., inflammatory bowel disease
900	TRICCACO	012			and Crohn's disease), and pain management.
667	HINGGA08	813	Activation of	Assays for the activation of transcription	Preferred indications include blood disorders (e.g., as
			transcription through	through the cAMP response element are	described below under "Immune Activity", "Blood-
			cAMP response	well-known in the art and may be used or	Related Disorders", and/or "Cardiovascular Disorders"),
			element in immune	routinely modified to assess the ability of	and infection (e.g., an infectious disease as described
			cells (such as T-cells).	polypeptides of the invention (including	below under "Infectious Disease"). Preferred
				antibodies and agonists or antagonists of	indications include autoimmune diseases (e.g., rheumatoid
				the invention) to increase cAMP and	arthritis, systemic lupus erythematosis, multiple sclerosis
				regulate CREB transcription factors, and	and/or as described below), immunodeficiencies (e.g., as
				modulate expression of genes involved in a	described below), boosting a T cell-mediated immune
				wide variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune

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			***	assays for transcription through the cAMP	response. Additional preferred indications include
				response element that may be used or	inflammation and inflammatory disorders. Highly
				routinely modified to test cAMP-response	seas
			4	element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Highly preferred
				agonists or antagonists of the invention)	indications include neoplasms and cancers, such as, for
				include assays disclosed in Berger et al.,	example, leukemia, lymphoma (e.g., T cell lymphoma.
		·		Gene 66:1-10 (1998); Cullen and Malm,	Burkitt's lymphoma, non-Hodgkins lymphoma. Hodgkin's
				Methods in Enzymol 216:362-368 (1992);	disease), melanoma, and prostate, breast, lung colon
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain liver and urinary
				85:6342-6346 (1988); Black et al., Virus	cancer. Other preferred indications include benion
				Genes 15(2):105-117 (1997); and	dysproliferative disorders and pre-neoplastic conditions
				Belkowski et al., J Immunol 161(2):659-	such as, for example, hyperplasia, metaplasia, and/or
				665 (1998), the contents of each of which	dysplasia. Preferred indications include anemia
				are herein incorporated by reference in its	pancytopenia, leukopenia, thrombocytopenia, acute
				entirety. T cells that may be used	lymphocytic anemia (ALL), plasmacytomas, multiple
				according to these assays are publicly	myeloma, arthritis, AIDS, granulomatous disease.
				available (e.g., through the ATCC).	inflammatory bowel disease, sensis, neutronenia
				Exemplary mouse T cells that may be used	neutrophilia, psoriasis, suppression of immine reactions to
				according to these assays include the	transplanted organs and tissues, hemophilia,
				CTLL cell line, which is a suspension	hypercoagulation, diabetes mellitus, endocarditis.
				culture of IL-2 dependent cytotoxic T	meningitis, Lyme Disease, and asthma and allergy.
6	0000000			cells.	
667	HNGGA68	813	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as I-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications

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				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992); Henthorn et al. Proc Natl Agad Sci 118 A	Highly preferred indications include neoplastic diseases
				85:6342-6346 (1988); and Black et al.,	(e.g., reuxenna, rymphoma, ana/or as described below under "Hyperproliferative Disorders"). Additionally.
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
-				incomposated by reference in its entirety. T	cancers, such as, for example, leukemia, lymphoma,
				cells that may be used according to these	incianoma, gnoma (e.g., mangnant gnoma), solid tumors, and prostate, breast, lung, colon, nancreatic, esonhageal
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
		·		may be used according to these assays	pre-neoplastic conditions, such as, for example,
-				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
-				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
565	HNGGA68	813	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.
			as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
<u></u>				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies

				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma
			.,	3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid nimors
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal
		-		of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysnlasia Preferred
				ATCC). Exemplary T cells that may be	indications include anemia nancytonenia leukonenia
				used according to these assays include the	thrombocytonenia Hodokin's disease acute lymphocytic
				NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma
				killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma arthritis. ADS granulomatons
				activity.	disease, inflammatory bowel disease, neutronenia
					neutrophilia, psoriasis, suppression of immune reactions to
					franchlanted organs and tissues hemoralilia
					hypercoagulation diabetes mellitus endocarditis
					meningitie I vme Dicease cardioc rangeflicion initiational
					asthma and allermy
					is infection (e.g., an infections disease as described below.
3					under "Infectious Disease").
<u> </u>	HNGGP65	814	Activation of	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			Hepatocyte ERK	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating hepatocyte cell
			Signaling Pathway	transduction that regulate cell proliferation	proliferation. An alternative highly preferred embodiment
				or differentiation are well known in the art	of the invention includes a method for inhibiting
				and may be used or routinely modified to	hepatocyte cell proliferation. A highly preferred
				assess the ability of polypeptides of the	embodiment of the invention includes a method for
				invention (including antibodies and	stimulating hepatocyte cell differentiation. An alternative
				ion) to	highly preferred embodiment of the invention includes a

skin), carpal cture). An obesity and/or Additional highly or alternatively, erred indications resistance. e disorders of the athies, muscular relude, hepatitis, degenerative or eases, fibrosis, slipidemia and Additional highly and cancers, such, and colon and also include ch, brain, and ns include benign stic conditions, asia, and/or	cell growth. of the lothelial cell the ndothelial rred od for A highly es a method e invention ing)
training the state of the state	ent of the invege endothelial embodiment of inhibiting encappoint of stimulating encappoints and inhibiting encappoints and inhib
below, especially of the urinary tract a tunnel syndrome and Dupuytren's con additional highly preferred indication complications associated with obesity preferred indications include weight Ic weight gain. Additional highly preferred indications musculoskeletal systems including my dystrophy, and/or as described herein. Additional highly preferred indication jaundice, gallstones, cirrhosis of the linecrotic liver disease, alcoholic liver disease, alcoholic liver disease, alcoholic liver disease, alcholesterol metabolism. The preferred indications include neoplasm as, hepatocarcinomas, other liver cancepanceatic cancer. Preferred indication prostate, breast, lung, esophageal, stourinary cancer. Other preferred indication prostate, for example, hyperplasia, metalysplasia,	A highly preferred embodiment of the includes a method for stimulating endot An alternative highly preferred emboding invention includes a method for inhibiting growth. A highly preferred embodim invention includes a method for stimulated proliferation. An alternative highly embodiment of the invention includes a inhibiting endothelial cell proliferation. preferred embodiment of the invention if for stimulating apoptosis of endothelial alternative highly preferred embodimen includes a method for inhibiting (e.g., deceived).
below, especially of the tunnel syndrome and Du additional highly preferr complications associated preferred indications inc weight gain. Additional systems dystrophy, and/or as dess Additional highly preferr jaundice, gallstones, cirrl necrotic liver disease, alk liver regeneration, metab chlolesterol metabolism. preferred indications incl as, hepatocarcinomas, oth pancreatic cancer. Prefer prostate, breast, lung, es urinary cancer. Other pre dysproliferative disorders such as, for example, hyp dysplasia.	A highly includes a me An alternative invention inc growth. A invention inc cell proliferat embodiment inhibiting enc preferred emb for stimulatin alternative hig includes a me
	8 kinase assays regulate cell apoptosis are nay be used or s the ability of on (including untagonists of r inhibit cell d apoptosis. and p38 kinase routinely 38 kinase-tides of the tides of the dides
	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and
	Kinase assa for signal trapoliferation well known routinely m polypeptide antibodies at the invention proliferation Exemplary activity that modified to induced activity invention (i)
	of I Cell p38 or ling
	Activation of Endothelial Cell JINK Signaling Pathway.
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agonists or antagonists of the invention)	embodiment of the invention includes a method for
include the assays disclosed in Forrer et	stimulating (e.g., increasing) endothelial cell activation.
al., Biol Chem 379(8-9):1101-1110	An alternative highly preferred embodiment of the
(1998); Gupta et al., Exp Cell Res 247(2):	invention includes a method for inhibiting (e.g.,
495-504 (1999); Kyriakis JM, Biochem	decreasing) the activation of and/or inactivating
Soc Symp 64:29-48 (1999); Chang and	endothelial cells. A highly preferred embodiment of
Karin, Nature 410(6824):37-40 (2001);	ludes a
and Cobb MH, Prog Biophys Mol Biol	angiogenisis. An alternative highly preferred embodiment
71(3-4):479-500 (1999); the contents of	of the invention includes a method for inhibiting
each of which are herein incorporated by	angiogenesis. A highly preferred embodiment of the
reference in its entirety. Endothelial cells	invention includes a method for reducing cardiac
that may be used according to these assays	hypertrophy. An alternative highly preferred embodiment
are publicly available (e.g., through the	of the invention includes a method for inducing cardiac
ATCC). Exemplary endothelial cells that	hypertrophy. Highly preferred indications include
may be used according to these assays	neoplastic diseases (e.g., as described below under
include human umbilical vein endothelial	"Hyperproliferative Disorders"), and disorders of the
cells (HUVEC), which are endothelial	cardiovascular system (e.g. heart disease, congestive heart
cells which line venous blood vessels, and	failure, hypertension, aortic stenosis, cardiomyonathy
are involved in functions that include, but	Valvular regurgitation, left ventricular dvsfunction
are not limited to, angiogenesis, vascular	atherosclerosis and atherosclerotic vascular disease
permeability, vascular tone, and immune	diabetic nephropathy, intracardiac shunt, cardiac
cell extravasation.	hypertrophy, myocardial infarction, chronic hemodynamic
	overload, and/or as described below under
	"Cardiovascular Disorders"). Highly preferred indications
	include cardiovascular, endothelial and/or angiogenic
	disorders (e.g., systemic disorders that affect vessels such
	as diabetes mellitus, as well as diseases of the vessels
	themselves, such as of the arteries, capillaries, veins and/or
	lymphatics). Highly preferred are indications that
	stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms
	and cancer, such as, Kaposi's sarcoma, hemangioma
	(capillary and cavernous), glomus tumors, telangiectasia

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bacillary angiomatosis, hemangioendothelioma,	angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver, and urinary	cancer. Preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions,	such as, for example, hyperplasia, metaplasia, and/or	dysplasia. Highly preferred indications also include	arterial disease, such as, atherosclerosis, hypertension,	coronary artery disease, inflammatory vasculitides,	Reynaud's disease and Reynaud's phenomenom,	aneurysms, restenosis; venous and lymphatic disorders	such as thrombophlebitis, lymphangitis, and lymphedema;	and other vascular disorders such as peripheral vascular	disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue	(e.g., vascular injury such as, injury resulting from balloon	angioplasty, and atheroschlerotic lesions), implant	fixation, scarring, ischemia reperfusion injury, rheumatoid	arthritis, cerebrovascular disease, renal diseases such as	acute renal failure, and osteoporosis. Additional highly	preferred indications include stroke, graft rejection,	diabetic or other retinopathies, thrombotic and coagulative	disorders, vascularitis, lymph angiogenesis, sexual	disorders, age-related macular degeneration, and treatment	/prevention of endometriosis and related conditions.	Additional highly preferred indications include fibromas,		vascular disease. Preferred indications include blood	disorders (e.g., as described below under "Immune	Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"). Preferred indications include	autoimmune diseases (e.g., rheumatoid arthritis, systemic	lupus erythematosis, multiple sclerosis and/or as described	below) and immunodeficiencies (e.g., as described below).	Additional preferred indications include inflammation and
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				inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease
HNGIV64	816	A action time of A J	.24	and Crohn's disease), and pain management.
±5 A 15 A 1	010	FDV Cignoling	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
		Dethusia	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
		Famway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
			or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
			and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
		_	assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
			invention (including antibodies and	differentiation. An alternative highly preferred
			agonists or antagonists of the invention) to	embodiment of the invention includes a method for
			promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
			activation, and differentiation. Exemplary	ū
			assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adinocyte activation. An
			used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
			kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of $\ell = \alpha$
			the invention (including antibodies and	decreasing) and/or inactivating adinocytes.
			agonists or antagonists of the invention)	rde
			include the assays disclosed in Forrer et	described below under "Endocrine Disorders")
			al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neonlastic
			(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
			Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
			(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension.
			64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
			410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
	-		Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
			(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
_			herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
			entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
			be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
			publicly available (e.g., through the	described below under "Infectious Disease").
			ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus.
			that may be used according to these assays	ation
			include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy.
			adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure.
		-	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
			cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic

and undergo a pre-adinomite of undergo	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.
	Additional highly preferred indications include weight loss
	or alternatively, weight gain. Additional highly
	preferred indications are complications associated with
	insulin resistance. Additional highly preferred
	indications are disorders of the musculoskeletal systems
	including myopathies, muscular dystrophy, and/or as
	described herein. Additional highly preferred
	indications include, hypertension, coronary artery disease,
	dyslipidemia, gallstones, osteoarthritis, degenerative
	arthritis, eating disorders, fibrosis, cachexia, and kidney
	diseases or disorders. Preferred indications include
	neoplasms and cancer, such as, lymphoma, leukemia and
	breast, colon, and kidney cancer. Additional preferred
	indications include melanoma, prostate, lung, pancreatic,
	esophageal, stomach, brain, liver, and urinary cancer.
	Highly preferred indications include lipomas and
	liposarcomas. Other preferred indications include benign
	dysproliferative disorders and pre-neoplastic conditions,
	such as, for example, hyperplasia, metaplasia, and/or
	dysplasia.

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Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke		Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Diseases"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as.
Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P et all	FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	activation of transcription 1 response element are the art and may be used or fied to assess the ability of f the invention (including agonists or antagonists of to modulate growth and itons. Exemplary assays for brough the API response ay be used or routinely t API-response element repetides of the invention bodies and agonists or the invention) include d in Berger et al., Gene ; Cullen and Malm,
Production of ICAM-1		Activation of transcription through AP1 response element in immune cells (such as T-cells).
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HNGJB41		HNGKT41
303		304

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				Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986- 4993 (1998); and Fraser et al., Eur J	leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis,
-				contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these recording to the recor	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, granulomatous disease, inflammatory
				through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is an IL-2 and IL-4 responsive suspension-	nower disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
, ,	, , , , , , , , , , , , , , , , , , ,			culture cell line.	
304	HNGK 141	8I8 	Activation of	Assays for the activation of transcription	A highly preferred embodiment of the invention
			CD28 response element	unrougn the CD28 response element are well-known in the art and may be used or	includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention
			in immune cells (such	routinely modified to assess the ability of	includes a method for inhibiting T cell proliferation. A
			as T-cells).	polypeptides of the invention (including	es a
				antibodies and agonists or antagonists of	method for activating T cells. An alternative highly
				in T cells. Exemplary assays for	preferred embodiment of the invention includes a method
				transcription through the CD28 response	A highly preferred embodiment of the invention includes a
				element that may be used or routinely	method for stimulating (e.g., increasing) IL-2 production.
				modified to test CD28-response element	An alternative highly preferred embodiment of the
				(including antibodies and agonists or	Invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly meferred
				antagonists of the invention) include	indications include inflammation and inflammatory
				assays disclosed in Berger et al., Gene	disorders. Highly preferred indications include
				66:1-10 (1998); Cullen and Malm,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				Methods in Enzymol 216:362-368 (1992);	lupus erythematosis, multiple sclerosis and/or as described
				Henthorn et al., Proc Natl Acad Sci USA	below), immunodeficiencies (e.g., as described below),
				85:6342-6346 (1988); McGuire and	boosting a T cell-mediated immune response, and
				Tacobelli, J Immunol 159(3):1319-1327	suppressing a T cell-mediated immune response. Highly
				(1997); Parra et al., J Immunol	preferred indications include neoplastic diseases (e.g.,

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melanoma, renal cell carcinoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g., metastatic melanoma), renal cell carcinoma (e.g., metastatic renal cell carcinoma), leukemia, lymphoma (e.g., T cell lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus crythematosis, multiple sclerosis and/or as described below) immunodeficiencies (e.g., as described below).
166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of
	Activation of transcription through NFAT response element in immune cells (such as T-cells).
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Actival transcri NFKB elemen	HNGKT41 818 Actival transcrip lemen	the invention) to regulate NFAT suppressing a T cell-mediated immune response, and transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response.	response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Genec. Other preferred indications include benign	", 8 8 m Cell ser et 1999); ontents ated hat	ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells. Assays for the activation of transcription through the NFKB response element are	well-known in the art and may be used or include blood disorders (e routinely modified to assess the ability of "Immune Activity", "Bloom and the statement of
		the tra exi im im	rour rour rour rour rour rour rour rour	Bic (2C (2C Bic al., and of c of c	ygno	element in immune rou

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				uanscription factors and modulate	described below), and immunodeficiencies (e.g., as	
				expression of immunomodulatory genes.	described below). An additional highly preferred	
				Exemplary assays for transcription through	indication is infection (e.g., AIDS, and/or an infectious	
				the NFKB response element that may be	disease as described below under "Infectious Disease")	
				used or rountinely modified to test NFKB-	Highly preferred indications include neoplastic diseases	
				response element activity of polypeptides	(e.g., melanoma, leukemia, lymphoma, and/or as described	-
				of the invention (including antibodies and	below under "Hyperproliferative Disorders"), Highly	
				agonists or antagonists of the invention)	preferred indications include neoplasms and cancers, such	
				include assays disclosed in Berger et al.,	as,melanoma, renal cell carcinoma, leukemia, lymphoma	
		·		Gene 66:1-10 (1998); Cullen and Malm,	and prostate, breast, lung, colon, pancreatic, esophageal,	
				Methods in Enzymol 216:362-368 (1992);	stomach, brain, liver and urinary cancer. Other preferred	
				Henthorn et al., Proc Natl Acad Sci USA	indications include benign dysproliferative disorders and	
			***	85:6342-6346 (1988); Black et al., Virus	pre-neoplastic conditions, such as, for example.	
	·			Gnes 15(2):105-117 (1997); and Fraser et	hyperplasia, metaplasia, and/or dysplasia. Preferred	
				al., 29(3):838-844 (1999), the contents of	indications also include anemia, pancytopenia, leukopenia,	
				each of which are herein incorporated by	thrombocytopenia, Hodgkin's disease, acute lymphocytic	
				reference in its entirety. T cells that may	anemia (ALL), plasmacytomas, multiple myeloma.	
				be used according to these assays are	Burkitt's lymphoma, arthritis, AIDS, granulomatous	
				publicly available (e.g., through the	disease, inflammatory bowel disease, sepsis, neutropenia.	
				ATCC). Exemplary human T cells that	neutrophilia, psoriasis, hemophilia, hypercoagulation.	
		-		may be used according to these assays	diabetes mellitus, endocarditis, meningitis, Lyme Disease.	
				include the SUPT cell line, which is a	suppression of immune reactions to transplanted organs	
				suspension culture of IL-2 and IL-4	asthma and allergy.	
				responsive T cells.		_
304	HNGKT41	818	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a	T
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha	
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of	
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,	
			as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications	
				(including antibodies and agonists or	include blood disorders (e.g., as described below under	
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or	
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications	
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,	
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple	
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies	
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated	
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated	

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				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
		···· • · · · · · · · · · · · · · · · ·		and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
		-		368 (1992); Henthorn et al., Proc Nati	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Senson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				38/3 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
	*			12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,
				used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,
				killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel disease, neutropenia,
		·			neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
20,	The County of	0.0			under "Infectious Disease").
e G	HNGMW45	819	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription through	through the PEPCK promoter are well-	An additional highly preferred indication is a complication
			the PEPCK promoter in	known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			hepatocytes	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
				polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to activate the PEPCK	neuropathy, nerve disease and nerve damage (e.g., due to
	-			promoter in a reporter construct and	diabetic neuropathy), blood vessel blockage, heart disease,
				regulate liver gluconeogenesis. Exemplary	stroke, impotence (e.g., due to diabetic neuropathy or
				assays for regulation of transcription	blood vessel blockage), seizures, mental confusion,

through the PEPCK promoter that may be	drowsiness, nonketotic hyneralycemic-hynerosmolar
used or routinely modified to test for	coma, cardiovascular disease (e.g., heart disease
PEPCK promoter activity (in hepatocytes)	atherosclerosis, microvascular disease, hypertension
of polypeptides of the invention (including	stroke, and other diseases and disorders as described in the
antibodies and agonists or antagonists of	"Cardiovascular Disorders" section below), dyslipidemia,
the invention) include assays disclosed in	endocrine disorders (as described in the "Endocrine
Berger et al., Gene 66:1-10 (1998); Cullen	Disorders" section below), neuropathy, vision impairment
and Malm, Methods in Enzymol 216:362-	(e.g., diabetic retinopathy and blindness), ulcers and
368 (1992); Henthorn et al., Proc Natl	impaired wound healing, infection (e.g., an infectious
Acad Sci USA 85:6342-6346 (1988);	diseases or disorders as described in the "Infectious
Lochhead et al., Diabetes 49(6):896-903	Diseases" section below, especially of the urinary tract and
(2000); and Yeagley et al., J Biol Chem	skin), carpal tunnel syndrome and Dupuytren's
275(23):17814-17820 (2000), the contents	contracture). An additional highly preferred indication
of each of which is herein incorporated by	is obesity and/or complications associated with obesity.
reference in its entirety. Hepatocyte cells	Additional highly preferred indications include weight loss
that may be used according to these assays	or alternatively, weight pain. Additional highly
are publicly available (e.g., through the	nlicatio
ATCC) and/or may be routinely generated.	insulin resistance
Exemplary liver hepatoma cells that may	ordere of th
be used according to these assays include	including myonathise muscular dustrouby, and one
H4lle cells, which contain a tyrosine amino	described herein
 transferase that is inducible with	indications include alycogen storage disease (e.g.
glucocorticoids, insulin, or cAMP	olvogenoses) henatitis galletones circhosis of the lister
derivatives.	degenerative or negrotic liver disease alooksis il IIVer,
	diseases, fibrosis, liver regeneration, metabolic diseases
	dyslibidemia and cholesterol metabolism and
	hepatocarcinomas. Highly preferred indications
	rders (e.g.,
	"Immune Activity", "Cardiovascular Disorders", and/or
	"Blood-Related Disorders"), immune disorders (e.g., as
	described below under "Immune Activity"), infection (e.g.,
	an infectious disease and/or disorder as described below
	under "Infectious Disease"), endocrine disorders (e.g., as
	described below under "Endocrine Disorders"), and neural
	disorders (e.g., as described below under "Neural Activity
	and Neurological Diseases"). Additional
	preferred indications include neoplastic diseases (e.g., as

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	<u> </u>				
					described below under "Hyperproliterative Disorders"). Dreferred indications include negative and sources and
					as, leukemia, lymphoma, prostate, breast, lung, colon,
				~ 	pancreatic, esophageal, stomach, brain, and urinary cancer.
					A highly preferred indication is liver cancer. Other
					preferred indications include benign dysproliferative
					disorders and pre-neoplastic conditions, such as, for
306	HNGNK44	820	Production of TNF	TNE FMAT Assays for	A highly professed amb discost
) -	alnha hy dendritic cells	imminomodulatory proteins and bu	_
			cition of audin	interior included and process produced by	includes a method for inhibiting (e.g., decreasing) TNF
				activated macrophages, I cells, tibroblasts,	alpha production. An alternative highly preferred
				smooth muscle, and other cell types that	embodiment of the invention includes a method for
		· .		exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
				well known in the art and may be used or	as described below under "Immune Activity", "Blood-
				routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders")
				polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
				antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis.
				the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
				immunomodulation, modulate	below), immunodeficiencies (e.g., as described below).
				inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
				assays that test for immunomodulatory	Suppressing a T cell-mediated immine response
				proteins evaluate the production of	Additional highly preferred indications include
				cytokines such as tumor necrosis factor	inflammation and inflammatory disorders and treating
				alpha (TNFa), and the induction or	joint damage in patients with rheumatoid arthritis. An
				inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
				response. Such assays that may be used or	
				routinely modified to test	leukemia, lymphoma, and/or as described below under
				immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
				polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
				antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
				the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
				Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
				4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
				"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
-				Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
				al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,

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pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and
(1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the upregulation of cell surface markers, such
	Upregulation of CD152 and activation of T cells
	850
	HNGNK44
	900

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				as (1) 150 and the activities of T cells	
-				Such assays that may be used or routinely	esoupageal stomach brain liver and minary concerns
				modified to test immunomodulatory	Other preferred indications include benion dysproliferative
			**	activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
		-	.,	antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
				77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis.
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
30/	HNGN053	821	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple

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				related genes in many cell types.	sclerosis and/or as described below). immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, leukemia, lymphoma, melanoma, glioma
				3873 (1994); and Black et al., Virus Genes	(e.g., malignant glioma), solid tumors, and prostate,
				12(2):105-117 (1997), the content of each	breast, lung, colon, pancreatic, esophageal, stomach,
				of which are herein incorporated by	brain, liver and urinary cancer. Other preferred indications
				reference in its entirety. Human T cells	include benign dysproliferative disorders and pre-
				that may be used according to these assays	neoplastic conditions, such as, for example, hyperplasia,
				are publicly available (e.g., through the	metaplasia, and/or dysplasia. Preferred indications
				ATCC). Exemplary human T cells that	include anemia, pancytopenia, leukopenia,
				may be used according to these assays	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				include the JURKAT cell line, which is a	anemia (ALL), plasmacytomas, multiple myeloma,
	-			suspension culture of leukemia cells that	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				produce IL-2 when stimulated.	disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
000	Pordorar	000			under "Infectious Disease").
208 	CZIAONH	778	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,

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			the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
			transcription factors and modulate gene	cancer. Other preferred indications include benign
			expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
			cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
			transcription through the GAS response	dysplasia. Preferred indications include autoimmune
			element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
			modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
			activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
			(including antibodies and agonists or	boosting a T cell-mediated immune response, and
			antagonists of the invention) include	suppressing a T cell-mediated immune response.
			assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
			66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
			Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
			Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
			85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
			Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
			Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
			4587 (1995), the contents of each of which	and/or an infectious disease as described below under
			are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
			entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
			may be used according to these assays are	include anemia, pancytopenia, leukopenia,
			publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
			ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
			used according to these assays include the	granulomatous disease, inflammatory bowel disease,
			CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
			culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
			cells.	hemophilia, hypercoagulation, diabetes mellitus,
				endocarditis, meningitis, Lyme Disease, and asthma and
308 HNGPJ25	822	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
		transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing). TNF alpha
	_	serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
		in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
		as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
			(including antibodies and agonists or	include blood disorders (e.g., as described below under
			antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
			the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications

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				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
		·····		Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
			•	cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia
		-		with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma.
					Burkitt's lymphoma, arthritis. AIDS, granulomatous
	***********				disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
	10140141				under "Infectious Disease").
308 808	HNGP325	778	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription of Malic	of Malic Enzyme are well-known in the art	An additional highly preferred indication is a complication
		<u>-</u>	Enzyme in adipocytes	and may be used or routinely modified to	associated with diabetes (e.g., diabetic retinopathy,
				assess the ability of polypeptides of the	diabetic nephropathy, kidney disease (e.g., renal failure,
				invention (including antibodies and	nephropathy and/or other diseases and disorders as

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				agonists or antagonists of the invention) to	described in the "Renal Disorders" section below), diabetic
				regulate transcription of Malic Enzyme, a	neuropathy, nerve disease and nerve damage (e.g., due to
				key enzyme in lipogenesis. Malic enzyme	diabetic neuropathy), blood vessel blockage, heart disease.
				is involved in lipogenesisand its expression	stroke, impotence (e.g., due to diabetic neuropathy or
				is stimulted by insulin. ME promoter	blood vessel blockage), seizures, mental confusion
				contains two direct repeat (DR1)- like	drowsiness, nonketotic hyperglycemic-hyperosmolar
				elements MEp and MEd identified as	coma, cardiovascular disease (e.g., heart disease.
				putative PPAR response elements. ME	atherosclerosis, microvascular disease, hypertension.
				promoter may also responds to AP1 and	stroke, and other diseases and disorders as described in the
				other transcription factors. Exemplary	"Cardiovascular Disorders" section below), dyslinidemia
				assays that may be used or routinely	endocrine disorders (as described in the "Endocrine
·-				modified to test for regulation of	Disorders" section below), neuropathy, vision impairment
				transcription of Malic Enzyme (in	(e.g., diabetic retinopathy and blindness) ulcers and
				adipoocytes) by polypeptides of the	impaired wound healing, and infection (e.g., infectious
				invention (including antibodies and	diseases and disorders as described in the "Infections
				agonists or antagonists of the invention)	Diseases" section below, especially of the urinary tract and
				include assays disclosed in: Streeper, R.S.,	skin), carpal tunnel syndrome and Dupuytren's
			-	et al., Mol Endocrinol, 12(11):1778-91	contracture). An additional highly preferred
				(1998); Garcia-Jimenez, C., et al., Mol	obesit
-			-	Endocrinol, 8(10):1361-9 (1994); Barroso,	obesity. Additional highly preferred indications include
_				I., et al., J Biol Chem, 274(25):17997-8004	weight loss or alternatively, weight gain. Aditional
				(1999); Ijpenberg, A., et al., J Biol Chem,	tions ass
				272(32):20108-20117 (1997); Berger, et	with insulin resistance.
				al., Gene 66:1-10 (1988); and, Cullen, B.,	
	-11			et al., Methods in Enzymol. 216:362-368	
				(1992), the contents of each of which is	
				herein incorporated by reference in its	
				entirety. Hepatocytes that may be used	
				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				hepatocytes that may be used according to	
				these assays includes the H4IIE rat liver	
				hepatoma cell line.	
505	HNHEN82	823	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			P13 Kinase Signalling	an GSK-3 assays, for PI3 kinase signal	includes a method for increasing adipocyte survival An
			Fathway	transduction that regulate glucose	alternative highly preferred embodiment of the invention

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metabolism and cell survival are well-	includes a method for december adjace adjace a
known in the art and may be used or	preferred embodiment of the invention includes a method
 routinely modified to assess the ability of	for stimulating adipocyte proliferation. An alternative
polypeptides of the invention (including	highly preferred embodiment of the invention includes a
antibodies and agonists or antagonists of	method for inhibiting adipocyte proliferation. A
the invention) to promote or inhibit	s
glucose metabolism and cell survival.	for stimulating adipocyte differentiation. An alternative
Exemplary assays for PI3 kinase activity	highly preferred embodiment of the invention includes a
that may be used or routinely modified to	method for inhibiting adipocyte differentiation. Highly
test PI3 kinase-induced activity of	S (e
polypeptides of the invention (including	described below under "Endocrine Disorders").
antibodies and agonists or antagonists of	Preferred indications include neoplastic diseases (e.g.,
the invention) include assays disclosed in	lipomas, liposarcomas, and/or as described below under
Forrer et al., Biol Chem 379(8-9):1101-	"Hyperproliferative Disorders"), blood disorders (e.g.,
1110 (1998); Nikoulina et al., Diabetes	hypertension, congestive heart failure, blood vessel
49(2):263-271 (2000); and Schreyer et al.,	blockage, heart disease, stroke, impotence and/or as
Diabetes 48(8):1662-1666 (1999), the	described below under "Immune Activity".
contents of each of which are herein	"Cardiovascular Disorders", and/or "Blood-Related
incorporated by reference in its entirety.	Disorders"), immune disorders (e.g., as described below
Mouse adipocyte cells that may be used	under "Immune Activity"), neural disorders (e.g., as
according to these assays are publicly	described below under "Neural Activity and Neurological
available (e.g., through the ATCC).	Diseases"), and infection (e.g., as described below under
Exemplary mouse adipocyte cells that may	"Infectious Disease"). A highly preferred indication
be used according to these assays include	₹
3T3-L1 cells. 3T3-L1 is an adherent	indication is a complication associated with diabetes (e.g.,
mouse preadipocyte cell line that is a	diabetic retinopathy, diabetic nephropathy, kidney disease
continous substrain of 3T3 fibroblast cells	(e.g., renal failure, nephropathy and/or other diseases and
developed through clonal isolation and	disorders as described in the "Renal Disorders" section
undergo a pre-adipocyte to adipose-like	below), diabetic neuropathy, nerve disease and nerve
conversion under appropriate	damage (e.g, due to diabetic neuropathy), blood vessel
differentiation conditions known in the art.	blockage, heart disease, stroke, impotence (e.g., due to
	diabetic neuropathy or blood vessel blockage), seizures,
	mental confusion, drowsiness, nonketotic hyperglycemic-
	hyperosmolar coma, cardiovascular disease (e.g., heart
	disease, atherosclerosis, microvascular disease,
	hypertension, stroke, and other diseases and disorders as
	described in the "Cardiovascular Disorders" section

			below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Highly preferred indications include
			neoplasms and cancer, such as, lipoma, liposarcoma, lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and preneoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
310 HNHFE71 824	Activation of Adipocyte Pl3 Kinase Signalling Pathway	Kinase assay. Kinase assays, for example an GSK-3 assays, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including	A highly preferred embodiment of the invention includes a method for increasing adipocyte survival An alternative highly preferred embodiment of the invention includes a method for decreasing adipocyte survival. A preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a

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the invention) to promote or inhibit	neferred embodiment of the invention includes a mathod
glucose metabolism and cell survival.	for stimulating adinocyte differentiation. An alternative
Exemplary assays for PI3 kinase activity	highly preferred embodiment of the invention includes a
that may be used or routinely modified to	method for inhibiting adipocyte differentiation. Highly
test PI3 kinase-induced activity of	rs (e
polypeptides of the invention (including	described below under "Endocrine Disorders").
antibodies and agonists or antagonists of	Preferred indications include neoplastic diseases (e.g.,
the invention) include assays disclosed in	lipomas, liposarcomas, and/or as described below under
Forrer et al., Biol Chem 379(8-9):1101-	"Hyperproliferative Disorders"), blood disorders (e.g.,
1110 (1998); Nikoulina et al., Diabetes	hypertension, congestive heart failure, blood vessel
49(2):263-271 (2000); and Schreyer et al.,	blockage, heart disease, stroke, impotence and/or as
Diabetes 48(8):1662-1666 (1999), the	described below under "Immune Activity",
contents of each of which are herein	"Cardiovascular Disorders", and/or "Blood-Related
incorporated by reference in its entirety.	Disorders"), immune disorders (e.g., as described below
Mouse adipocyte cells that may be used	under "Immune Activity"), neural disorders (e.g., as
according to these assays are publicly	described below under "Neural Activity and Neurological
available (e.g., through the ATCC).	Diseases"), and infection (e.g., as described below under
Exemplary mouse adipocyte cells that may	"Infectious Disease"). A highly preferred indication
be used according to these assays include	⋖
3T3-L1 cells. 3T3-L1 is an adherent	licatior
mouse preadipocyte cell line that is a	diabetic retinopathy, diabetic nephropathy, kidney disease
continous substrain of 3T3 fibroblast cells	(e.g., renal failure, nephropathy and/or other diseases and
developed through clonal isolation and	disorders as described in the "Renal Disorders" section
undergo a pre-adipocyte to adipose-like	below), diabetic neuropathy, nerve disease and nerve
conversion under appropriate	damage (e.g, due to diabetic neuropathy), blood vessel
differentiation conditions known in the art.	blockage, heart disease, stroke, impotence (e.g., due to
	diabetic neuropathy or blood vessel blockage), seizures,
	mental confusion, drowsiness, nonketotic hyperglycemic-
	hyperosmolar coma, cardiovascular disease (e.g., heart
	disease, atherosclerosis, microvascular disease,
	hypertension, stroke, and other diseases and disorders as
	described in the "Cardiovascular Disorders" section
	below), dyslipidemia, endocrine disorders (as described in
	the "Endocrine Disorders" section below), neuropathy,
	vision impairment (e.g., diabetic retinopathy and
 	blindness), ulcers and impaired wound healing, infection
	(e.g., infectious diseases and disorders as described in the

HNHEF1 824 Calcium flux in monocytes) Calcium flux in monocytes) Calcium flux in monocytes) Calcium flux are immune cells (such as monocytes) Continely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell

				need or routinely modified to moon	
				יייייייייייייייייייייייייייייייייייייי	
-				calcium flux in immune cells (such as	
				monocytes) include assays disclosed in:	
•				Chan, CC, et al., J Pharmacol Exp Ther,	
				269(3):891-896 (1994); Andersson, K, et	
				al., Cytokine, 12(12):1784-1787 (2000);	
<u>-</u>				Scully, SP, et al., J Clin Invest, 74(2) 589-	
				599 (1984); and, Sullivan, E, et al.,	
				Methods Mol Biol, 114:125-133 (1999),	
				the contents of each of which is herein	
				incorporated by reference in its entirety.	
				Cells that may be used according to these	
				assays are publicly available (e.g., through	
				the ATCC) and/or may be routinely	
				generated. Exemplary cells that may be	
				used according to these assays include the	
				THP-1 monocyte cell line	
311 HNF	HNHGK22	825	Activation of	Account the state of the state	
		70	ACUVACION OI	Assays for the activation of transcription	A preferred embodiment of the invention includes a
-			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
				(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis.
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
<u> </u>				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
-				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,

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Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Total that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectious disease as described below under "Infectious Disease.")	ion tion of of of of of of of of of see of s
Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety, cells that may be used according to thesa assays are publicly available (e.g., throuthe ATCC). Exemplary mouse T cells to may be used according to these assays include the CTLL cell line, which is an 2 dependent suspension culture of T cell with cytotoxic activity.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include
	Activation of transcription through GAS response element in immune cells (such as T-cells).
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			assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications
			Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
			Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
			85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
			Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
			Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
			4587 (1995), the contents of each of which	and/or an infectious disease as described below under
			are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
			entirety. Exemplary human T cells, such	is idiopathic pulmonary fibrosis. Preferred indications
		-	as the MOLT4 cell line, that may be used	include anemia, pancytopenia, leukopenia,
			according to these assays are publicly	thrombocytopenia, acute lymphocytic anemia (ALL),
			available (e.g., through the ATCC).	plasmacytomas, multiple myeloma, arthritis, AIDS,
				granulomatous disease, inflammatory bowel disease,
				sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				immune reactions to transplanted organs and tissues.
				hemophilia, hypercoagulation, diabetes mellitus,
				endocarditis, meningitis. Lyme Disease, and asthma and
+				allergy.
313 HNHKS19	827	Protection from	Caspase Apoptosis Rescue. Assays for	A highly preferred embodiment of the invention
		Endothelial Cell	caspase apoptosis rescue are well known in	includes a method for stimulating endothelial cell growth
		Apoptosis.	the art and may be used or routinely	An alternative highly preferred embodiment of the
			modified to assess the ability of the	invention includes a method for intitities and all 11:11:11
		_	nolymentides of the invention (including	invention includes a method for inhibiting endothelial cell
			polypeptides of the invention (including	growth. A highly preferred embodiment of the
			antibodies and agonists or antagonists of	invention includes a method for stimulating endothelial
		.,_	the invention) to inhibit caspase protease-	cell proliferation. An alternative highly preferred
			mediated apoptosis. Exemplary assays for	embodiment of the invention includes a method for
			caspase apoptosis that may be used or	inhibiting endothelial cell proliferation. A highly
			routinely modified to test caspase	preferred embodiment of the invention includes a method
			apoptosis rescue of polypeptides of the	for stimulating endothelial cell growth. An alternative
			invention (including antibodies and	highly preferred embodiment of the invention includes a
			agonists or antagonists of the invention)	method for inhibiting endothelial cell growth.
			include the assays disclosed in Romeo et	incl
			al., Cardiovasc Res 45(3): 788-794 (2000);	method for stimulating apoptosis of endothelial cells. An
			Messmer et al., Br J Pharmacol 127(7):	alternative highly preferred embodiment of the invention
-			1633-1640 (1999); and J Atheroscler	includes a method for inhibiting (e.g., decreasing)
			Thromb 3(2): 75-80 (1996); the contents of	apoptosis of endothelial cells. A highly preferred

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embodiment of the invention includes a method for stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for	reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and	disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular	usease, utabetic nephroparty, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred	indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries.	veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization.	indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer such as Kanosi's sarcoma hamancians.	(capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiogarcoma, Highly preferred indications of the language of th	include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary
each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary	endothelial cells that may be used according to these assays include bovine aortic endothelial cells (bAEC), which are an example of endothelial cells which line blood vessels and are involved in functions	that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.						

			-		uyspioliticialive disorders and pre-neoplastic conditions,
					such as, for example, hyperplasia, metaplasia, and/or
					dysplasia. Highly preferred indications also include
					arterial disease, such as, atherosclerosis, hypertension,
					coronary artery disease, inflammatory vasculitides,
					Reynaud's disease and Reynaud's phenomenom,
					aneurysms, restenosis; venous and lymphatic disorders
					such as thrombophlebitis, lymphangitis, and lymphedema;
					and other vascular disorders such as peripheral vascular
		···			disease, and cancer. Highly preferred indications also
					include trauma such as wounds, burns, and injured tissue
					(e.g., vascular injury such as, injury resulting from balloon
					angioplasty, and atheroschlerotic lesions), implant
					fixation, scarring, ischemia reperfusion injury, rheumatoid
					arthritis, cerebrovascular disease, renal diseases such as
					acute renal failure, and osteoporosis. Additional highly
					ī
					diabetic or other retinopathies, thrombotic and coagulative
					disorders, vascularitis, lymph angiogenesis, sexual
					disorders, age-related macular degeneration, and treatment
					/prevention of endometriosis and related conditions.
					Additional highly preferred indications include fibromas,
				,	heart disease, cardiac arrest, heart valve disease, and
					vascular disease. Preferred indications include blood
					disorders (e.g., as described below under "Immune
					Activity", "Blood-Related Disorders", and/or
					"Cardiovascular Disorders"). Preferred indications include
					autoimmune diseases (e.g., rheumatoid arthritis, systemic
					lupus erythematosis, multiple sclerosis and/or as described
					below) and immunodeficiencies (e.g., as described below).
					Additional preferred indications include inflammation and
					inflammatory disorders (such as acute and chronic
					inflammatory diseases, e.g., inflammatory bowel disease
314	HNTRT17	828	Dendingtion of II 10 1		and Crohn's disease), and pain management.
;	1117111	070	domination of the 10 and		A highly preferred embodiment of the invention includes a
			downregulation or	immunomodulatory proteins produced by	method for stimulating the production of IL-10. An
			minime responses	activated I cells, B cells, and monocytes	alternative preferred embodiment of the invention

that exhibit anti-inflammatory activity and	includes a method for inhibiting the production of IL-10.
downregulate monocyte/macrophage	Highly preferred indications include inflammation and
function and expression of cytokines are	inflammatory disorders (e.g. inflammatory howel disease)
well known in the art and may be used or	An additional highly preferred indication includes
routinely modified to assess the ability of	inflammatory bowel disease. Additional highly
the polypeptides of the invention	preferred indications include blood disorders (e.g., as
(including antibodies and agonists or	described below under "Immune Activity" (e.g.
antagonists of the invention) to mediate	autoimmune disorders), "Blood-Related Disorders", and/or
immunomodulation, regulate inflammatory	"Cardiovascular Disorders"). Highly preferred indications
activities, and modulate immune cell	include autoimmune diseases (e.g., rheumatoid arrhritis
function and cytokine production.	systemic lupus erythematosis, multiple sclerosis and/or as
Exemplary assays that test for	described below) and immunodeficiencies (e.g. as
immunomodulatory proteins evaluate the	described below). Preferred indications include
production of cytokines, such as IL-10,	45
 and the downmodulation of immune	and/or as described below under "Hynernroliferative"
responses. Such assays that may be used	Disorders"), Preferred indications include neonlasms and
or routinely modified to test	cancers, such as, for example, leukemia, lymphoma
immunomodulatory activity of	melanoma, and prostate, breast ling colon paperestic
polypeptides of the invention (including	esophageal, stomach, brain, liver and urinary cancer
antibodies and agonists or antagonists of	Other preferred indications include benion dysproliferative
the invention) include the assays disclosed	disorders and pre-neoplastic conditions, such as, for
in Miraglia et al., J Biomolecular	example, hyperplasia, metaplasia, and/or dysplasia
Screening 4:193-204 (1999); Rowland et	Preferred indications include anemia, pancytonenia
al., "Lymphocytes: a practical approach"	leukopenia, thrombocytopenia, Hodgkin's disease, acute
Chapter 6:138-160 (2000); and Koning et	lymphocytic anemia (ALL), plasmacytomas, multiple
al., Cytokine 9(6):427-436 (1997), the	myeloma, Burkitt's lymphoma, Crohn's disease, arthritis
 contents of each of which are herein	AIDS, granulomatous disease, sepsis, neutropenia.
incorporated by reference in its entirety.	neutrophilia, psoriasis, suppression of immune reactions to
Human T cells that may be used according	transplanted organs and tissues, hemophilia.
to these assays may be isolated using	hypercoagulation, diabetes mellitus, endocarditis.
techniques disclosed herein or otherwise	meningitis, Lyme Disease, asthma and allerov
known in the art. Human T cells are	Se
primary human lymphocytes that mature in	described below under "Infectious Disease").
the thymus and express a T cell receptor	
 and CD3, CD4, or CD8. These cells	
mediate humoral or cell-mediated	
immunity and may be preactivated to	

				enhance responsiveness to immunomodulatory factors	
315	HNTMH79	829	Activation of	Assays for the activation of transcription	D. 5. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1.
		<u> </u>	two mooninging the	dissays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
			danscription unrough	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
			API response element	known in the art and may be used or	blood disorders (e.g., as described below under "Immune"
	 , .		in immune cells (such	routinely modified to assess the ability of	Activity", "Cardiovascular Disorders", and/or "Blood-
			as T-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious
				antibodies and agonists or antagonists of	disease as described below under "Infectious Disease")
				the invention) to modulate growth and	Highly preferred indications include autoimmine diseases
				other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lunus erythematosis
				transcription through the AP1 response	multiple sclerosis and/or as described below) and
				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
	,			modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia
				antagonists of the invention) include	lymphoma, and/or as described below under
				assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders") Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neonlasms and cancers such as
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast ling colon
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain liver and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benian
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis.
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukonenia
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety.	anemia (ALL), plasmacytomas, multiple myeloma
				Mouse T cells that may be used according	Burkitt's lymphoma, granulomatous disease, inflammatory
	•			to these assays are publicly available (e.g.,	bowel disease, sepsis, psoriasis, suppression of immine
				through the ATCC). Exemplary mouse T	reactions to transplanted organs and tissues, endocarditis
				cells that may be used according to these	meningitis, and Lyme Disease.
				assays include the HT2 cell line, which is	
				an IL-2 dependent suspension culture cell	
316	110 4 011	000		line that also responds to IL-4.	
210	HUABE31	830		IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			LFINgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			Cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the

cytokine. IFNg promotes TH1 and	inclu	
inhibits 1 HZ differentiation; promotes	of IFNg. Highly preferred indications include blood	
IgG2a and inhibits IgE secretion; induces	(e.g.,	
macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or	
MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral	
immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic	
T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis.	
of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").	
helper cell functions are well known in the	Highly preferred indications include autoimmune disease	
art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis.	
to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),	_
invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T	
agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-	_
mediate immunomodulation, regulate	mediated immune response. Additional highly preferred	
inflammatory activities, modulate TH2	indications include inflammation and inflammatory	
helper cell function, and/or mediate	disorders. Additional preferred indications include	
humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred	
Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia.	
immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under	
production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred	
gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for	
cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate.	
routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach.	
immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications	
polypeptides of the invention (including	include benign dysproliferative disorders and pre-	
antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,	
 the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications	
in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,	
Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic	
al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma.	
Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous	
J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia.	
Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to	
(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,	
15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,	
(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.	
of each of which are herein incorporated		

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			imminomodulatory activity of	hrain liver and uninary cancer Other preferred indications
			nolumentides of the insention (including	include benish disease items diseases and and
			polypepudes of the invention (including	include benign dysprollierative disorders and pre-
			antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
			the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
			in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
			Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
			Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
			J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
			Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
			(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
			15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
			(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
			of each of which are herein incorporated	.
			by reference in its entirety. Human T cells	
			that may be used according to these assays	
			may be isolated using techniques disclosed	
			herein or otherwise known in the art.	
			Human T cells are primary human	
			lymphocytes that mature in the thymus and	
			express a T Cell receptor and CD3, CD4,	
			or CD8. These cells mediate humoral or	
			cell-mediated immunity and may be	
			preactivated to enhance responsiveness to	
			immunomodulatory factors.	
318 HOACG07	832	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
		Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
		cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
			polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
			antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
			the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
			example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
			measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
			have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
			calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
			extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
			can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,

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				activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
				pathways and alterations in cell functions.	Stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below) disclinidemia
				Exemplary assays that may be used of routinely modified to measure calcium flux	cardiovascular Disorders, section below), dysupraenna, endocrine disorders (as described in the "Endocrine
		,		by polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Satin LS, et al., Endocrinology,	diseases and disorders as described in the "Infectious
				136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
				al., Endocrinology, 136(7):2960-6 (1995);	tunne
				Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
				3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
				Cell Calcium 1989 Nov-Dec;10(8):535-41	obesity. Additional highly preferred indications include
				(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include HITT15	
				Cells. HITT15 are an adherent epithelial	
				cell line established from Syrian hamster	
				islet cells transformed with SV40. These	
				cells express glucagon, somatostatin, and	
				glucocorticoid receptors. The cells secrete	
				insulin, which is stimulated by glucose and	
				glucagon and suppressed by somatostatin	
				or glucocorticoids. ATTC# CRL-1777	
				Refs: Lord and Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc. Natl. Acad.	
				Sci. USA 78: 4339-4343, 1981.	
319	HODAG07	833	Activation of	Assays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
			transcription through	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
			AP1 response element	known in the art and may be used or	blood disorders (e.g., as described below under "Immune
			in immune cells (such	routinely modified to assess the ability of	Activity", "Cardiovascular Disorders", and/or "Blood-
			as I-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious

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				antibodies and agonists or antagonists of the invention) to modulate growth and	disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases
				other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				uanscription unough the Arritespoinse element that may be used or routinely	inmulpre sericiosis and or as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
				assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
				may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
				2 dependent suspension-culture cell line	
-				with cytotoxic activity.	
320 H	HODBB70	834	Activation of	Assays for the activation of transcription	Preferred indications include blood disorders (e.g., as
			transcription through	through the cAMP response element are	described below under "Immune Activity", "Blood-
			cAMP response	well-known in the art and may be used or	Related Disorders", and/or "Cardiovascular Disorders"),
			element in immune	routinely modified to assess the ability of	and infection (e.g., an infectious disease as described
			cells (such as T-cells).	polypeptides of the invention (including	below under "Infectious Disease"). Preferred
				antibodies and agonists or antagonists of	indications include autoimmune diseases (e.g., rheumatoid
				the invention) to increase cAMP and	arthritis, systemic lupus erythematosis, multiple sclerosis
				regulate CREB transcription factors, and	and/or as described below), immunodeficiencies (e.g., as
		-		modulate expression of genes involved in a	described below), boosting a T cell-mediated immune
				wide variety of cell functions. Exemplary	response, and suppressing a 1 cell-mediated immune

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				assays for transcription through the cAMP	inc
				response element that may be used or	inflammation and inflammatory disorders. Highly
				routinely modified to test cAMP-response	preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Highly preferred
				agonists or antagonists of the invention)	indications include neoplasms and cancers, such as, for
•				include assays disclosed in Berger et al.,	example, leukemia, lymphoma (e.g., T cell lymphoma,
				Gene 66:1-10 (1998); Cullen and Malm,	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				Methods in Enzymol 216:362-368 (1992);	disease), melanoma, and prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver and urinary
				85:6342-6346 (1988); Black et al., Virus	cancer. Other preferred indications include benign
				Genes 15(2):105-117 (1997); and	dysproliferative disorders and pre-neoplastic conditions,
				Belkowski et al., J Immunol 161(2):659-	such as, for example, hyperplasia, metaplasia, and/or
				665 (1998), the contents of each of which	dysplasia. Preferred indications include anemia,
				are herein incorporated by reference in its	pancytopenia, leukopenia, thrombocytopenia, acute
				entirety. T cells that may be used	lymphocytic anemia (ALL), plasmacytomas, multiple
				according to these assays are publicly	myeloma, arthritis, AIDS, granulomatous disease,
				available (e.g., through the ATCC).	inflammatory bowel disease, sepsis, neutropenia,
				Exemplary mouse T cells that may be used	neutrophilia, psoriasis, suppression of immune reactions to
				according to these assays include the	transplanted organs and tissues, hemophilia,
				CTLL cell line, which is a suspension	hypercoagulation, diabetes mellitus, endocarditis,
				culture of IL-2 dependent cytotoxic T	meningitis, Lyme Disease, and asthma and allergy.
				cells.	
320	HODBB70	834	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription through	through the PEPCK promoter are well-	An additional highly preferred indication is a complication
			the PEPCK promoter in	known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			hepatocytes	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
				polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to activate the PEPCK	neuropathy, nerve disease and nerve damage (e.g., due to
				promoter in a reporter construct and	diabetic neuropathy), blood vessel blockage, heart disease,
				regulate liver gluconeogenesis. Exemplary	stroke, impotence (e.g., due to diabetic neuropathy or
				assays for regulation of transcription	blood vessel blockage), seizures, mental confusion,
				through the PEPCK promoter that may be	drowsiness, nonketotic hyperglycemic-hyperosmolar
				used or routinely modified to test for	coma, cardiovascular disease (e.g., heart disease,
				PEPCK promoter activity (in hepatocytes)	atherosclerosis, microvascular disease, hypertension,
				of polypeptides of the invention (including	stroke, and other diseases and disorders as described in the

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antibodies and agonists or antagonists of	"Cardiovascular Disorders" section below), dyslipidemia,
the invention) include assays disclosed in	endocrine disorders (as described in the "Endocrine
Berger et al., Gene 66:1-10 (1998); Cullen	Disorders" section below), neuropathy, vision impairment
and Malm, Methods in Enzymol 216:362-	(e.g., diabetic retinopathy and blindness), ulcers and
368 (1992); Henthorn et al., Proc Natl	impaired wound healing, infection (e.g., an infectious
Acad Sci USA 85:6342-6346 (1988);	diseases or disorders as described in the "Infectious
Lochhead et al., Diabetes 49(6):896-903	Diseases" section below, especially of the urinary tract and
(2000); and Yeagley et al., J Biol Chem	skin), carpal tunnel syndrome and Dupuytren's
275(23):17814-17820 (2000), the contents	contracture). An additional highly preferred indication
of each of which is herein incorporated by	is obesity and/or complications associated with obesity.
reference in its entirety. Hepatocyte cells	Additional highly preferred indications include weight loss
that may be used according to these assays	or alternatively, weight gain. Additional highly
are publicly available (e.g., through the	preferred indications are complications associated with
ATCC) and/or may be routinely generated.	insulin resistance. Additional highly preferred
Exemplary liver hepatoma cells that may	indications are disorders of the musculoskeletal systems
be used according to these assays include	including myopathies, muscular dystrophy, and/or as
H4lle cells, which contain a tyrosine amino	described herein. Additional highly preferred
transferase that is inducible with	indications include glycogen storage disease (e.g.,
glucocorticoids, insulin, or cAMP	glycogenoses), hepatitis, gallstones, cirrhosis of the liver,
derivatives.	degenerative or necrotic liver disease, alcoholic liver
	diseases, fibrosis, liver regeneration, metabolic disease,
	dyslipidemia and cholesterol metabolism, and
	hepatocarcinomas. Highly preferred indications
	include blood disorders (e.g., as described below under
	"Immune Activity", "Cardiovascular Disorders", and/or
	"Blood-Related Disorders"), immune disorders (e.g., as
	described below under "Immune Activity"), infection (e.g.,
	an infectious disease and/or disorder as described below
	under "Infectious Disease"), endocrine disorders (e.g., as
	described below under "Endocrine Disorders"), and neural
	disorders (e.g., as described below under "Neural Activity
	and Neurological Diseases"). Additional
	preferred indications include neoplastic diseases (e.g., as
	described below under "Hyperproliferative Disorders").
	Preferred indications include neoplasms and cancers, such
	as, leukemia, lymphoma, prostate, breast, lung, colon,
	pancreatic, esophageal, stomach, brain, and urinary cancer.

					A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative
					disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
321	HODBV05	835	Production of MCP-1	MCP-1 FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins that are	includes a method for stimulating (e.g., increasing) MCP-1
				produced by a large variety of cells and act	production. An alternative highly preferred embodiment of
				to induce chemotaxis and activation of	the invention includes a method for inhibiting (e.g.,
				monocytes and T cells are well known in	reducing) MCP-1 production. A highly preferred
				the art and may be used or routinely	indication is infection (e.g., an infectious disease as
				modified to assess the ability of	described below under "Infectious Disease"). Additional
				polypeptides of the invention (including	highly preferred indications include inflammation and
				antibodies and agonists or antagonists of	inflammatory disorders. Preferred indications include
				the invention) to mediate	blood disorders (e.g., as described below under "Immune
				immunomodulation, induce chemotaxis,	Activity", "Blood-Related Disorders", and/or
				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
				Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
				production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenía, neutrophilia, psoriasis,
-				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
				Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
				Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
				al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,
				contents of each of which are herein	pancreatic, esophageal, stomach, brain, liver, and urinary
				incorporated by reference in its entirety.	cancer. Other preferred indications include benign
				Human dendritic cells that may be used	dysproliferative disorders and pre-neoplastic conditions,

				according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation	such as, for example, hyperplasia, metaplasia, and/or dysplasia.
				and functional activities.	
322 H	HODCZ32	836	Activation of Natural Killer Cell ERK	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal	A highly preferred embodiment of the invention includes a method for stimulating natural killer cell
			Signaling Pathway.	transduction that regulate cell proliferation	proliferation. An alternative highly preferred embodiment
				or differentiation are well known in the art	of the invention includes a method for inhibiting natural
				and may be used or routinely modified to	killer cell proliferation. A highly preferred
				assess the ability of polypeptides of the	embodiment of the invention includes a method for
				invention (including antibodies and	stimulating natural killer cell differentiation. An
				agonists or antagonists of the invention) to	alternative highly preferred embodiment of the invention
				promote or innibit cell proliferation,	differentiation for inhibiting natural killer cell
				activation, and differentiation. Exemplary	differentiation. Highly preferred indications include
				assays for EKK kinase activity that may be used or routingly modified to test EDV	"Transment diseases (e.g., as described below under "Transmentiferation Diseases"). Pland diseases (2.g., 2.g., 2.
				used of foundingly intodiffed to test Erra	Tryper profilerative Disorders), prood disorders (e.g., as
				kinase-induced activity of polypeptides of	described below under "Immune Activity", "Cardianian Discretain", and (an immune Activity)
				ule invention (including antibodies and	Cardiovascular Disorders, and/or biood-related
				agonists or antagonists of the invention)	Disorders"), immune disorders (e.g., as described below
				include the assays disclosed in Forrer et	, as
				al., Biol Chem 379(8-9):1101-1110	described below under "Infectious Disease"). Preferred
				(1998); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., as described
				64:29-48 (1999); Chang and Karin, Nature	below under "Immune Activity", "Blood-Related
				410(6824):37-40 (2001); and Cobb MH,	Disorders", and/or "Cardiovascular Disorders"). Highly
			-	Prog Biophys Mol Biol 71(3-4):479-500	preferred indications include autoimmune diseases (e.g.,
				(1999); the contents of each of which are	rheumatoid arthritis, systemic lupus erythematosis,
				herein incorporated by reference in its	multiple sclerosis and/or as described below) and
			-	entirety. Natural killer cells that may be	immunodeficiencies (e.g., as described below). Additional
				used according to these assays are publicly	highly preferred indications include inflammation and
				available (e.g., through the ATCC).	inflammatory disorders. Highly preferred indications
				Exemplary natural killer cells that may be	also include cancers such as, kidney, melanoma, prostate,
				used according to these assays include the	breast, lung, colon, pancreatic, esophageal, stomach,
				human natural killer cell lines (for	brain, liver, urinary cancer, lymphoma and leukemias.

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:				example, NK-YT cells which have cytolytic and cytotoxic activity) or primary NK cells.	Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and allergies.
323	НОЕВК60	837	Insulin Secretion	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann N Y Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and,	etes mell is a com tinopath s., renal f sorders a disease, ypertens disease, ypertens as descril w), dyslij "Endocri vision im vision im ulcers a e.g., infecti e urinary tren's oreferred s associa
				Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents	weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated

324 HOFAA78 838 A	Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway	of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981. Kinase assay. Kinase assays, for Pf3 kinase an GSK-3 kinase assay, for Pf3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit Exemplary assays for Pf3 kinase activity that may be used or routinely modified to test Pf3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of anta	with insulin resistance. A highly preferred embodiment of the invention includes a method for increasing muscle cell survival. An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for decreasing muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell proliferation is inhibited. A preferred embodiment of the invention includes a method for stimulating muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is stimulated. An alternative muscle cell differentiation is stimulated. An alternative highly preferred embodiment of the invention includes a method for stimulated.
		the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes	method for inhibiting muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is inhibited. Highly preferred indications include disorders

	49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein incorporated by reference in its entirety. Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat myoblast cells that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuses to form multinucleated myotubes and striated	of the musculoskeletal system. Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), endocrine disorders (e.g., as described below under "Endocrine Disorders"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Infection (e.g., as described below under "Infections Disease"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication
	fibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment
		(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infections (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly

				preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal system including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions,
325 HOFNB74	839	Insulin Secretion	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Shimizu, H., et al., Endocr J, 47(3):261-9	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious

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			Lindociiioi, 13(0).1303-17 (1333),	skiil), caipai tuillici syllulolile allu Dupuyuell s
			Filipsson, K., et al., Ann N Y Acad Sci,	contracture). An additional highly preferred
			865:441-4 (1998); Olson, L.K., et al., J	indication is obesity and/or complications associated with
			Biol Chem, 271(28):16544-52 (1996); and,	obesity. Additional highly preferred indications include
			Miraglia S et. al., Journal of Biomolecular	weight loss or alternatively, weight gain. Aditional
			Screening, 4:193-204 (1999), the contents	highly preferred indications are complications associated
			of each of which is herein incorporated by	with insulin resistance.
			reference in its entirety. Pancreatic cells	
			that may be used according to these assays	
			are publicly available (e.g., through the	
			ATCC) and/or may be routinely generated.	
			Exemplary pancreatic cells that may be	
			used according to these assays include	
			HITT15 Cells. HITT15 are an adherent	
			epithelial cell line established from Syrian	
			hamster islet cells transformed with SV40.	
			These cells express glucagon,	
			somatostatin, and glucocorticoid receptors.	
	-		The cells secrete insulin, which is	
			stimulated by glucose and glucagon and	
			suppressed by somatostatin or	
			glucocorticoids. ATTC# CRL-1777	
			Refs: Lord and Ashcroft. Biochem. J. 219:	
			547-551; Santerre et al. Proc. Natl. Acad.	
			Sci. USA 78: 4339-4343, 1981.	
326 HOFNU55	840	Activation of	Assays for the activation of transcription	Preferred indications include blood disorders (e.g., as
		transcription through	through the cAMP response element are	described below under "Immune Activity", "Blood-
		cAMP response	well-known in the art and may be used or	Related Disorders", and/or "Cardiovascular Disorders"),
		element in immune	routinely modified to assess the ability of	and infection (e.g., an infectious disease as described
		cells (such as T-cells).	polypeptides of the invention (including	below under "Infectious Disease"). Preferred
			antibodies and agonists or antagonists of	indications include autoimmune diseases (e.g., rheumatoid
			the invention) to increase cAMP, bind to	arthritis, systemic lupus erythematosis, multiple sclerosis
			CREB transcription factor, and modulate	and/or as described below), immunodeficiencies (e.g., as
			expression of genes involved in a wide	described below), boosting a T cell-mediated immune
			variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune
			assays for transcription through the cAMP	is inc
		والمراجعة	response element that may be used or	initialimation and initalimatory disorders. Highly

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				routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2	preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, ALDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
327 HOC	НОСВЕОІ	841	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm,	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as,

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			Methods in Enzymol 210:302-308 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line.	reukemia, lymphoma, prostate, oreast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
327 HOGBF01	841	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and differentiation and	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred embodiment of midication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cellmediated immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred indications include inflammation and inflammatory disorders. Additional highly preferred indications include inflammation and inflammatory

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				Exemplary assays that test for	neoplastic diseases (e.g. myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
	·			the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
7.1				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
327	HOGBF01	841		IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	inch
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
				macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
				MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
				immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
				T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
				of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").

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helper cell functions are well known in the	Highly preferred indications include autoimmune disease
 art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
 agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
inflammatory activities, modulate TH2	indications include inflammation and inflammatory
helper cell function, and/or mediate	disorders. Additional preferred indications include
 humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
 Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
polypeptides of the invention (including	include benign dysproliferative disorders and pre-
antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
of each of which are herein incorporated	
by reference in its entirety. Human T cells	
that may be used according to these assays	
may be isolated using techniques disclosed	
herein or otherwise known in the art.	
 Human T cells are primary human	
lymphocytes that mature in the thymus and	
express a T Cell receptor and CD3, CD4,	
or CD8. These cells mediate humoral or	

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				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
	HORBS82	842	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
			,	or differentiation are well known in the art	
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred
				agonists or antagonists of the invention) to	embodiment of the invention includes a method for
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
				agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
				entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
				be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
				publicly available (e.g., through the	described below under "Infectious Disease").
				ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
				that may be used according to these assays	additional highly preferred indication is a complication
				include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
				adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
				is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
				cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic

			blood vessel blockage), seizures, mental confusion,	drowsiness, nonketotic hyperglycemic-hyperosmolar	coma, cardiovascular disease (e.g., heart disease,	atherosclerosis, microvascular disease, hypertension,	stroke, and other diseases and disorders as described in the	"Cardiovascular Disorders" section below), dyslipidemia,	endocrine disorders (as described in the "Endocrine	Disorders" section below), neuropathy, vision impairment	(e.g., diabetic retinopathy and blindness), ulcers and	impaired wound healing, infection (e.g., infectious	diseases and disorders as described in the "Infectious	Diseases" section below (particularly of the urinary tract	and skin). An additional highly preferred indication is	id/oi	Additional highly preferred indications include weight loss	or alternatively, weight gain. Additional highly	preferred indications are complications associated with	insulin resistance. Additional highly preferred	indications are disorders of the musculoskeletal systems	including myopathies, muscular dystrophy, and/or as	described herein. Additional highly preferred	indications include, hypertension, coronary artery disease,	dyslipidemia, gallstones, osteoarthritis, degenerative	arthritis, eating disorders, fibrosis, cachexia, and kidney	diseases or disorders. Preferred indications include	neoplasms and cancer, such as, lymphoma, leukemia and	breast, colon, and kidney cancer. Additional preferred	indications include melanoma, prostate, lung, pancreatic,	esophageal, stomach, brain, liver, and urinary cancer.	Highly preferred indications include lipomas and	liposarcomas. Other preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions,	such as, for example, hyperplasia, metaplasia, and/or	dysplasia.
and undergo a pre-adipocyte to adipose-	like conversion under appropriate	differentiation conditions known in the art.																																		
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Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.							
Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to	regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues	throughout the body, and their activation via immunoglobulin E-antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease.	Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell tumor survival. Exemplary assays for caspase apoptosis that may be used or	routinely modified to test capase apoptosis activity induced by polypeptides of the invention (including antibodies and agonists or antagonists of the invention)	include the assays disclosed in: Masuda A, et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000); Lee et al., FFBS 1 ett 485(2-3): 122-126 (2000): Nor	et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immine cells that	may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC
Regulation of apoptosis of immune cells (such as mast cells).							
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				human mast cell line.	
329	HORBV76	843	Production of ICAM-1	Assays for measuring expression of	Preferred embodiments of the invention include using
				ICAM-1 are well-known in the art and	polypeptides of the invention (or antibodies, agonists, or
				may be used or routinely modified to	antagonists thereof) in detection, diagnosis, prevention,
				assess the ability of polynentides of the	and/or treatment of Inflammation. Vascular Disease.
				invention (including antihodies and	Athereoceletoeic Dectenosis and Stroke
				invention (including antibodies and	Autoroboticiosis, trosteriosis, una ou oro
				agonists or antagonists of the invention) to	
				regulate ICAM-1 expression. Exemplary	
				assays that may be used or routinely	
				modified to measure ICAM-1 expression	
				include assays disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281 (2001); and,	
				Miyamoto K, et al., Am J Pathol,	
				156(5):1733-1739 (2000), the contents of	
				each of which is herein incorporated by	
				reference in its entirety. Cells that may be	
				used according to these assays are publicly	
				ovoilable (e.g. through the ATCC) and/or	
				available (c.g., unough me AICC) and of	
				may be routinely generated. Exemplary	
				cells that may be used according to these	
				assays include microvascular endothelial	
				cells (MVEC).	
330	HOSDO75	844	Regulation of apoptosis	Caspase Apoptosis. Assays for caspase	A highly preferred indication is diabetes mellitus.
			in pancreatic beta cells.	apoptosis are well known in the art and	An additional highly preferred indication is a complication
				may be used or routinely modified to	associated with diabetes (e.g., diabetic retinopathy,
				assess the ability of polypeptides of the	diabetic nephropathy, kidney disease (e.g., renal failure,
				invention (including antibodies and	nephropathy and/or other diseases and disorders as
				agonists or antagonists of the invention) to	described in the "Renal Disorders" section below), diabetic
				promote caspase protease-mediated	neuropathy, nerve disease and nerve damage (e.g., due to
				apoptosis. Apoptosis in pancreatic beta is	diabetic neuropathy), blood vessel blockage, heart disease,
				associated with induction and progression	stroke, impotence (e.g., due to diabetic neuropathy or
				of diabetes. Exemplary assays for	blood vessel blockage), seizures, mental confusion,
				caspase apoptosis that may be used or	drowsiness, nonketotic hyperglycemic-hyperosmolar
				routinely modified to test capase apoptosis	coma, cardiovascular disease (e.g., heart disease,
				activity of polypeptides of the invention	atherosclerosis, microvascular disease, hypertension,
				(including antibodies and agonists or	stroke, and other diseases and disorders as described in the
				antagonists of the invention) include the	"Cardiovascular Disorders" section below), dyslipidemia,

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cell growth and differentiation are well	invention includes a method for stimulating T cell
known in the art and may be used or	expansion. An alternative highly preferred embodiment of
routinely modified to assess the ability of	the invention includes a method for inhibiting T cell
polypeptides of the invention (including	expansion. A highly preferred embodiment of the
antibodies and agonists or antagonists of	invention includes a method for stimulating T cell
the invention) to mediate	differentiation. In a specific embodiment, this method
immunomodulation, promote immune cell	stimulates T cell differentiation into effector cells. An
growth and differentiation, and/or mediate	alternative highly preferred embodiment of the invention
humoral or cell-mediated immunity.	includes a method for inhibiting T cell differentiation. In a
 Exemplary assays that test for	specific embodiment, this method inhibits the
immunomodulatory proteins evaluate the	differentiation of T cells into effector cells. Highly
production of cytokines, such as IL-2, and	preferred indications include neoplastic diseases (e.g.,
the activation of T cells. Such assays that	melanoma, renal cell carcinoma, leukemia, lymphoma,
may be used or routinely modified to test	and/or as described below under "Hyperproliferative
immunomodulatory activity of	Disorders"). Highly preferred indications include
polypeptides of the invention (including	neoplasms, such as, for example, melanoma (e.g.,
antibodies and agonists or antagonists of	metastatic melanoma), renal cell carcinoma (e.g.,
the invention) include the assays disclosed	metastatic renal cell carcinoma), leukemia, lymphoma
in Miraglia et al., J Biomolecular	(e.g., T cell lymphoma), and prostate, breast, lung, colon,
Screening 4:193-204 (1999); Rowland et	pancreatic, esophageal, stomach, brain, liver, ovarian, and
al., "Lymphocytes: a practical approach"	urinary cancer. Other preferred indications include benign
Chapter 6:138-160 (2000); Laduda et al.,	dysproliferative disorders and pre-neoplastic conditions,
Immunology 94(4):496-502 (1998); and	such as, for example, hyperplasia, metaplasia, and/or
Powell et al., Immunol Rev 165:287-300	dysplasia. A highly preferred indication is infection (e.g.,
 (1998), the contents of each of which are	an infectious disease as described below under "Infectious
herein incorporated by reference in its	Disease"). A highly preferred indication is AIDS and HIV
entirety. Human T cells that may be used	infection. Additional highly preferred indications include
according to these assays may be isolated	suppression of immune reactions to transplanted organs
using techniques disclosed herein or	, u
otherwise known in the art. Human T cells	paraparesis. Preferred indications include blood
are primary human lymphocytes that	disorders (e.g., as described below under "Immune
mature in the thymus and express a T cell	Activity", "Blood-Related Disorders", and/or
receptor and CD3, CD4, or CD8. These	"Cardiovascular Disorders"). Preferred indications include
cells mediate humoral or cell-mediated	autoimmune diseases (e.g., rheumatoid arthritis, systemic
immunity and may be preactivated to	lupus erythematosis, multiple sclerosis and/or as described
enhance responsiveness to	below), immunodeficiencies (e.g., as described below),
Immunomodulatory factors.	organ and ussue transpiant rejection. Additional

preferred indications include inflammation and inflammatory disorders. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, Non-Hodgkin's lymphoma, Kaposi's sarcoma arthritis, granulomatous disease, inflammatory bowel disease, Hepatitis (e.g. Hepatitis C), sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of inflammation, infection, allergy, asthma, autoimmunity, and cancer.
	Kinase assays, for example kinase assays for members of the MAP kinase family (including p38, JAK, and ERK) are well known in the art and may be used or routinely modified to assess the ability of a polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, differentiation., and/or cytokine production in immune cells such as T-cells. Exemplary assays for MAP kinase family members that may be used or routinely modified to test polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Rincon M., Curr Opin Immunol; 13(3):339-345 (2001); Wang LH, et al., J Immunol, 162(7):3897-3904 (1999); Sakamoto H, et al., J Biol Chem, 275(46):35857-35862 (2000), the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells (for example, T-cells) that may be used according to these assays include the mouse CTLL cell line.
	Proliferation, differentiation, and/or cytokine production in immune cells (such as T-cells).
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A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal	immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g.	rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cell-mediated immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred indications include inflammation and inflammatory	disorders. Additional highly preferred indications include asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer.	disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to
IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production p and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression in		ated by rmones y be used e ability including onists of		the invention activity of polypeptuces of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol is 158:2919-2925 (1997), the contents of
Production of IL-6				
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				each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture,	transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
				which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	
334	HOUCA21	848		IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFINgamma using a 1 cells	role in the immune system and is considered to be a proinflammatory	includes a method for summating the production of tring. An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	invention includes a method for inhibiting the production
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
				macrophage activation; and increases MHC expression. Assays for	Activity, Biood-related Disorders, and/or "Cardiovascular Disorders"), and infection (e.g., viral
				immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
				T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
				of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
				helper cell functions are well known in the	Highly preferred indications include autoimmune disease
				art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
				invention (including antibodies and	mmunodefliciency (e.g., as described below), boosting a 1 cell-mediated immine response and suppressing a T cell.
				mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
				inflammatory activities, modulate TH2	indications include inflammation and inflammatory
				helper cell function, and/or mediate	disorders. Additional preferred indications include
				humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
				Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
				immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
				production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
				gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
				cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
				routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
				immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications

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335 HOUDE92	849	Activation of transcription through	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. Assays for the activation of transcription through the AP1 response element are	include benign dysproliferative disorders and preneoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy. Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Hyperproliferative Disorders").
		as T-cells).	routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or	Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia,

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lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammatory disorders. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP and regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary assays for transcription through the cAMP response element that may be used or routinely modified to test cAMP-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,
	Activation of transcription through cAMP response element in immune cells (such as T-cells).
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		Methods in Enzymol 210:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85.6342-6346 (1988): Serfling et al.	cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as for example, hyperplasia, metaplasia, and/or

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dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Autoimmunity, Allergy and Asthma
Biochim Biophys Acta 1498(1):1-18 (2000); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gri G, et al., Biol Chem, 273(11):6431-6438 (1998); Pyatt DW, et al., Cell Biol Toxicol 2000;16(1):41-51 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA
	Activation of transcription through NFKB response element in immune cells (such as B-cells).
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	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Neurological Diseases and Disorders (e.g. Alzheimer's Disease, Parkinson's Disease, Brain Cancer, Seizures).
85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary immune cells that may be used according to these assays include the Reh B-cell line.	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of neuronal genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gill JS, et al., Neurobiol Dis, 7(4):448-461 (2000); Tamatani M, et al., J Biol Chem, 274(13):8531-8538 (1999); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-
	Activation of transcription through NFKB response element in neuronal cells (such as SKNMC cells).
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			810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its	
			entirety. Neuronal cells that may be used according to these assays are publicly	
			available (e.g., through the ATCC).	
			Exemplary neuronal cells that may be used	
			according to these assays include the SKNMC neuronal cell line.	
335 HOUDE92	849	Activation of	Assays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
		transcription through	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
		AP1 response element	well-known in the art and may be used or	blood disorders (e.g., as described below under "Immune
		in immune cells (such	routinely modified to assess the ability of	Activity", "Cardiovascular Disorders", and/or "Blood-
-		as T-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious
			antibodies and agonists or antagonists of	disease as described below under "Infectious Disease").
			the invention) to modulate growth and	Highly preferred indications include autoimmune diseases
			other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
			transcription through the AP1 response	multiple sclerosis and/or as described below) and
			element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
			modified to test AP1-response element	highly preferred indications include inflammation and
			activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
			(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
			antagonists of the invention) include	lymphoma, and/or as described below under
			assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
			66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
			Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
			Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
			85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
			Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
			Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
			4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
			Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
			contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
	lot r'		incorporated by reference in its entirety.	anemia (ALL), plasmacytomas, multiple myeloma,
			Human T cells that may be used according	Burkitt's lymphoma, granulomatous disease, inflammatory
			to these assays are publicly available (e.g.,	bowel disease, sepsis, psoriasis, suppression of immune
			Inrough the AICC). Exemplary numan 1	reactions to transplanted organs and tissues, endocardius,

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			cells that may be used according to these	meningitis, and Lyme Disease.
			assays include the SUPT cell line, which is	
			an IL-2 and IL-4 responsive suspension-	
335 HOUDE92	849	Activation of	Assays for the activation of transcription	A highly preferred embodiment of the invention
		transcription through	through the CD28 response element are	includes a method for stimulating T cell proliferation. An
		CD28 response element	well-known in the art and may be used or	alternative highly preferred embodiment of the invention
		in immune cells (such	routinely modified to assess the ability of	includes a method for inhibiting T cell proliferation. A
		as T-cells).	polypeptides of the invention (including	highly preferred embodiment of the invention includes a
			antibodies and agonists or antagonists of	method for activating T cells. An alternative highly
			the invention) to stimulate IL-2 expression	preferred embodiment of the invention includes a method
			in T cells. Exemplary assays for	for inhibiting the activation of and/or inactivating T cells.
			transcription through the CD28 response	A highly preferred embodiment of the invention includes a
			element that may be used or routinely	method for stimulating (e.g., increasing) IL-2 production.
			modified to test CD28-response element	An alternative highly preferred embodiment of the
			activity of polypeptides of the invention	invention includes a method for inhibiting (e.g., reducing)
			(including antibodies and agonists or	IL-2 production. Additional highly preferred
			antagonists of the invention) include	indications include inflammation and inflammatory
			assays disclosed in Berger et al., Gene	disorders. Highly preferred indications include
			66.1-10 (1998); Cullen and Malm,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
			Methods in Enzymol 216:362-368 (1992);	lupus erythematosis, multiple sclerosis and/or as described
			Henthorn et al., Proc Natl Acad Sci USA	below), immunodeficiencies (e.g., as described below),
			85:6342-6346 (1988); McGuire and	boosting a T cell-mediated immune response, and
			Iacobelli, J Immunol 159(3):1319-1327	suppressing a T cell-mediated immune response. Highly
			(1997); Parra et al., J Immunol	preferred indications include neoplastic diseases (e.g.,
			166(4):2437-2443 (2001); and Butscher et	melanoma, renal cell carcinoma, leukemia, lymphoma,
			al., J Biol Chem 3(1):552-560 (1998), the	and/or as described below under "Hyperproliferative
			contents of each of which are herein	Disorders"). Highly preferred indications include
			incorporated by reference in its entirety. T	neoplasms and cancers, such as, for example, melanoma
			cells that may be used according to these	(e.g., metastatic melanoma), renal cell carcinoma (e.g.,
			assays are publicly available (e.g., through	metastatic renal cell carcinoma), leukemia, lymphoma
			the ATCC). Exemplary human T cells that	(e.g., T cell lymphoma), and prostate, breast, lung, colon,
			may be used according to these assays	pancreatic, esophageal, stomach, brain, liver and urinary
			include the SUPT cell line, which is a	cancer. Other preferred indications include benign
			suspension culture of IL-2 and IL-4	dysproliferative disorders and pre-neoplastic conditions,
			responsive T cells.	such as, for example, hyperplasia, metaplasia, and/or
				uyspiasia. A lightly preferred incheaton inches

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infection (e.g., AIDS, tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications include suppression of immune reactions to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Diseases"). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary
·	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,
	Activation of transcription through NFAT response element in immune cells (such as T-cells).
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				Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
				Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
				85:6342-6346 (1988); Serfling et al.,	such as, for example, hyperplasia, metaplasia, and/or
				Biochim Biophys Acta 1498(1):1-18	dysplasia. Preferred indications also include anemia,
				(2000); De Boer et al., Int J Biochem Cell	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				Biol 31(10):1221-1236 (1999); Fraser et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., Eur J Immunol 29(3):838-844 (1999);	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				and Yeseen et al., J Biol Chem	granulomatous disease, inflammatory bowel disease,
				268(19):14285-14293 (1993), the contents	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				of each of which are herein incorporated	immune reactions to transplanted organs and tissues,
				by reference in its entirety. T cells that	hemophilia, hypercoagulation, diabetes mellitus,
				may be used according to these assays are	endocarditis, meningitis, Lyme Disease, asthma and
				publicly available (e.g., through the	allergy.
			-	ATCC). Exemplary human T cells that	
				may be used according to these assays	
				include the SUPT cell line, which is a	
				suspension culture of IL-2 and IL-4	
				responsive T cells.	
335	HOUDE92	849	Activation of	Assays for the activation of transcription	A highly preferred indication is allergy.
			transcription through	through the Signal Transducers and	Another highly preferred indication is asthma.
			STAT6 response	Activators of Transcription (STAT6)	Additional highly preferred indications include
			element in immune	response element are well-known in the art	inflammation and inflammatory disorders.
			cells (such as T-cells).	and may be used or routinely modified to	Preferred indications include blood disorders (e.g., as
				assess the ability of polypeptides of the	described below under "Immune Activity", "Blood-
				invention (including antibodies and	Related Disorders", and/or "Cardiovascular Disorders").
				agonists or antagonists of the invention) to	Preferred indications include autoimmune diseases (e.g.,
				regulate STAT6 transcription factors and	rheumatoid arthritis, systemic lupus erythematosis,
•				modulate the expression of multiple genes.	multiple sclerosis and/or as described below) and
				Exemplary assays for transcription through	immunodeficiencies (e.g., as described below).
				the STAT6 response element that may be	Preferred indications include neoplastic diseases (e.g.,
				used or routinely modified to test STAT6	leukemia, lymphoma, melanoma, and/or as described
				response element activity of the	below under "Hyperproliferative Disorders"). Preferred
				polypeptides of the invention (including	indications include neoplasms and cancers, such as,
				antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and prostate, breast,
				the invention) include assays disclosed in	lung, colon, pancreatic, esophageal, stomach, brain, liver
				Berger et al., Gene 66:1-10 (1998); Cullen	and urinary cancer. Other preferred indications include
				and Malm, Methods in Enzymol 216:362-	benign dysproliferative disorders and pre-neoplastic

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			368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Georas et al., Blood 92(12):4529-4538 (1998); Moffatt et al., Transplantation 69(7):1521-1523 (2000); Curiel et al., Eur J Immunol 27(8):1982-1987 (1997); and Masuda et al., J Biol Chem 275(38):29331-29337 (2000), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the SUPT cell line, which is a suspension	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
335 HOUDE92	849	Activation of transcription through NFKB response element in immune cells (such as T-cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example,

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			-	al 29(3):838-844 (1999), the contents of	indications also include anemia, pancytopenia, leukopenia,
				each of which are herein incorporated by	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				reference in its entirety. T cells that may	anemia (ALL), plasmacytomas, multiple myeloma,
				be used according to these assays are	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				publicly available (e.g., through the	disease, inflammatory bowel disease, sepsis, neutropenia,
				ATCC). Exemplary human T cells that	neutrophilia, psoriasis, hemophilia, hypercoagulation,
		•		may be used according to these assays	diabetes mellitus, endocarditis, meningitis, Lyme Disease,
				include the SUPT cell line, which is a	suppression of immune reactions to transplanted organs,
				suspension culture of IL-2 and IL-4	asthma and allergy.
				responsive T cells.	
335	HOUDE92	849	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
		_		expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
			-	of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,

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			publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below myellow arthrights and allergy.
336 HOUDR07	850	Activation of Skeletal Muscle Cell ERK Signalling Pathway	Kinase assay. Kinase assays, for examplek Elk-1 kinase assays, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500	Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders") and disorders of the musculoskeletal system. Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Infectious Disease"). An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis microvascular disease

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	•	,		herein incorporated by reference in its entirety. Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat myoblast cells that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuses to form multinucleated myotubes and striated fibers after culture in differentiation media.	hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications are associated with obesity. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease, cardiac arrest, heart valve disease, and vascular disease, cardiac arrest, heart failure, cachexia, myxomas, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Highly preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.
337	HOUED72	851	Activation of transcription through API response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases

				other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				transcription through the AP1 response	multiple sclerosis and/or as described below) and
				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
				assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
				may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
				2 dependent suspension-culture cell line	
				with cytotoxic activity.	t many many management of the second of the
338 I	HOUFS04	852	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	re
				transcription through the GAS response	dyspiasia. Preferred indications include autoimmune

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				element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4 cell line, that may be used	diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia,
338	HOUFS04	852	Activation of transcription through NFKB response element in immune	available (e.g., through the ATCC). Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of	plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or
			cells (such as T-cells).	polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides	"Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described

		of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).	below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune
338 HOUFS04	 Upregulation of T cells and activation of T cells	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired immunoresponses. Assays for immunoresponses. Assays for immunomodulatory proteins important in the maintenance of T cell homeostasis and expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, maintain T cell homeostasis, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,

				Call of the Call o	Line of the state
				iniminational proteins evaluate une	inginy preferred indications include neopiasins and
				upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
			-	(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.
				antagonists of the invention) include, for	Preferred indications include anemia, pancytopenia,
				example, the assays disclosed in Miraglia	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				et al., J Biomolecular Screening 4:193-204	lymphocytic anemia (ALL), plasmacytomas, multiple
				(1999); Rowland et al., "Lymphocytes: a	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				practical approach" Chapter 6:138-160	granulomatous disease, inflammatory bowel disease,
				(2000); McCoy et al., Immunol Cell Biol	sepsis, neutropenia, neutrophilia, psoriasis, immune
		· ·		77(1):1-10 (1999); Oostervegal et al., Curr	reactions to transplanted organs and tissues, hemophilia,
				Opin Immunol 11(3):294-300 (1999); and	hypercoagulation, diabetes mellitus, endocarditis,
				Saito T, Curr Opin Immunol 10(3):313-	meningitis, Lyme Disease, inflammation and
				321 (1998), the contents of each of which	inflammatory disorders, and asthma and allergy. An
				are herein incorporated by reference in its	additional preferred indication is infection (e.g., as
				entirety. Human T cells that may be used	described below under "Infectious Disease").
				according to these assays may be isolated	
				using techniques disclosed herein or	
				otherwise known in the art. Human T cells	
				are primary human lymphocytes that	
				mature in the thymus and express a T Cell	
				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to imminomodulatory factors	
339	HOUHI25	853	Activation of	Assays for the activation of transcription	A highly preferred indication is allergy.
			transcription through	through the Signal Transducers and	Another highly preferred indication is asthma.
			STAT6 response	Activators of Transcription (STAT6)	Additional highly preferred indications include
			element in immune	response element are well-known in the art	inflammation and inflammatory disorders.
			cells (such as T-cells).	and may be used or routinely modified to	Preferred indications include blood disorders (e.g., as
				assess the ability of polypeptides of the	described below under "Immune Activity", "Blood-
				invention (including antibodies and	Related Disorders", and/or "Cardiovascular Disorders").
				agonists or antagonists of the invention) to	Preferred indications include autoimmune diseases (e.g.,

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				regulate STAT6 transcription factors and	rheumatoid arthritis, systemic lupus erythematosis,
				modulate the expression of multiple genes.	multiple sclerosis and/or as described below) and
				Exemplary assays for transcription through	immunodeficiencies (e.g., as described below).
				the STAT6 response element that may be	Preferred indications include neoplastic diseases (e.g.,
				used or routinely modified to test STAT6	leukemia, lymphoma, melanoma, and/or as described
				response element activity of the	below under "Hyperproliferative Disorders"). Preferred
				polypeptides of the invention (including	indications include neoplasms and cancers, such as,
				antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and prostate, breast,
				the invention) include assays disclosed in	lung, colon, pancreatic, esophageal, stomach, brain, liver
				Berger et al., Gene 66:1-10 (1998); Cullen	and urinary cancer. Other preferred indications include
				and Malm, Methods in Enzymol 216:362-	benign dysproliferative disorders and pre-neoplastic
				368 (1992); Henthorn et al., Proc Natl	conditions, such as, for example, hyperplasia, metaplasia,
				Acad Sci USA 85:6342-6346 (1988);	and/or dysplasia. Preferred indications
				Georas et al., Blood 92(12):4529-4538	include anemia, pancytopenia, leukopenia,
				(1998); Moffatt et al., Transplantation	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				69(7):1521-1523 (2000); Curiel et al., Eur	anemia (ALL), plasmacytomas, multiple myeloma,
				J Immunol 27(8):1982-1987 (1997); and	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				Masuda et al., J Biol Chem	disease, inflammatory bowel disease, sepsis, neutropenia,
				275(38):29331-29337 (2000), the contents	neutrophilia, psoriasis, suppression of immune reactions to
				of each of which are herein incorporated	transplanted organs and tissues, hemophilia,
				by reference in its entirety. T cells that	litus, endo
				may be used according to these assays are	meningitis, and Lyme Disease. An additional
				publicly available (e.g., through the	preferred indication is infection (e.g., an infectious disease
-				ATCC). Exemplary T cells that may be	as described below under "Infectious Disease").
				used according to these assays include the	
				SUPT cell line, which is a suspension	
				culture of IL-2 and IL-4 responsive T cells.	
340	HOVBD85	854	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple

				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immine response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,
				used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,
				killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
341	HPCAB41	855	Activation of	Kinase assay. JNK and p38 kinase assays	A highly preferred embodiment of the invention
			Endothelial Cell p38 or	for signal transduction that regulate cell	includes a method for stimulating endothelial cell growth.
			JNK Signaling	proliferation, activation, or apoptosis are	An alternative highly preferred embodiment of the
			Pathway.	well known in the art and may be used or	invention includes a method for inhibiting endothelial cell
				routinely modified to assess the ability of	growth. A highly preferred embodiment of the
				polypeptides of the invention (including	invention includes a method for stimulating endothelial
				antibodies and agonists or antagonists of	cell proliferation. An alternative highly preferred

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inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing)	apoptosis of endouteiral cens. A miginy protection embodiment of the invention includes a method for stimulating (e.g., increasing) endothelial cell activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) the activation of and/or inactivating endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating	angiogensis. An atternative inginy preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, disheric grantly cardiac	hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization.
the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the	agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001);	and Cobb MH, Prog Biophys Moi Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular	permeability, vascular tone, and immune cell extravasation.

Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma,	angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides,	Reynaud's disease and Reynaud's phenomenom, aneurysms, restenosis, venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and lymphedema; and other vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood

342 HPCAL26	856	Activation of transcription through GAS response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and	disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory diseases, e.g., inflammatory bowel disease and Crohn's diseases, e.g., inflammatory bowel diseases and Crohn's diseases, and pain management. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, fiseases), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysplasia. Preferred indications include benign dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response, and suppressing a T cell-mediated immune response, and clude blood disorders. Highly preferred indications include blood disorders, and infection (e.g., viral infections, tuberculosis, infections associated below winder "Temune Activity", "Blood-Related Disorders", and/or infections, tuberculosis, infections associated with chronic
		Mar.	Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary mouse T cells that	granulomatosus disease and manginalit osteopolosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications

				and arrange of the second of t	include anemia nancutonenia leukonenia
				iliay ue useu accoluliig to tilese assays are	include discussing pariety to period, controlled to the controlled
				publicly available (e.g., through the	thrombocytopenia, acute lymphocytic aneilia (ALL),
		·		ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
				used according to these assays include the	granulomatous disease, inflammatory bowel disease,
				CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
				cells.	hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
343	HPEAD23	857	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
			Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
				example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
				measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
		·		have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
				calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
				extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
				can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,
				activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
				pathways and alterations in cell functions.	stroke, and other diseases and disorders as described in the
				Exemplary assays that may be used or	"Cardiovascular Disorders" section below), dyslipidemia,
				routinely modified to measure calcium flux	endocrine disorders (as described in the "Endocrine
				by polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Satin LS, et al., Endocrinology,	diseases and disorders as described in the "Infectious
				136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
				al., Endocrinology, 136(7):2960-6 (1995);	tunne
				Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
				3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
		,		Cell Calcium 1989 Nov-Dec;10(8):535-41	cations i
				(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.

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а н	trare as described below under "Hyperproliferative Disorders"), as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune bility of Activity", "Cardiovascular Disorders", and/or "Blood-luding disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or
according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-
	Activation of transcription through API response element in immune cells (such as T-cells).
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dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. Additional preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach,
Immunol 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test
	Production of IFNgamma using a T cells
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				immunomodulatory activity of nolymentides of the invention (including	brain, liver and urinary cancer. Other preferred indications include benion dysmoliferative disorders and pre-
				antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
				the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
				in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
				Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
				Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
				Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
				(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
				15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
				(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
				of each of which are herein incorporated	
				by reference in its entirety. Human T cells	
				that may be used according to these assays	
				may be isolated using techniques disclosed	
				herein or otherwise known in the art.	
				Human T cells are primary human	
				lymphocytes that mature in the thymus and	
				express a T Cell receptor and CD3, CD4,	
				or CD8. These cells mediate humoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
345	HPFCI36	859	Production of	MIP-1alpha FMAT. Assays for	A highly preferred embodiment of the invention
			MIP1alpha	immunomodulatory proteins produced by	includes a method for stimulating MIP1a production. An
-				activated dendritic cells that upregulate	alternative highly preferred embodiment of the invention
				monocyte/macrophage and T cell	includes a method for inhibiting (e.g., reducing) MIP1a
				chemotaxis are well known in the art and	production. A highly preferred indication is infection
				may be used or routinely modified to	(e.g., an infectious disease as described below under
				assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
				invention (including antibodies and	blood disorders (e.g., as described below under "Immune
				agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
-				mediate immunomodulation, modulate	"Cardiovascular Disorders"). Highly preferred indications
				chemotaxis, and modulate T cell	include autoimmune diseases (e.g., rheumatoid arthritis,
				differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as

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				tor immunomodulatory proteins evaluate	described below) and infinitionalities (e.g., as
				the production of chemokines, such as	described below). Additional highly preferred indications
				macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
				(MIP-1a), and the activation of	Preferred indications also include anemia, pancytopenia,
				monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				assays that may be used or routinely	lymphocytic anemia (ALL), plasmacytomas, multiple
				modified to test immunomodulatory and	myeloma, Burkitt's lymphoma, arthritis, AIDS,
				chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
				invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
				include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
				J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
				204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
				a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
				(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
				Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
				al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
				Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
				2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
				Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
				each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
				reference in its entirety. Human dendritic	dysplasia.
				cells that may be used according to these	
				assays may be isolated using techniques	
				disclosed herein or otherwise known in the	
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
-				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
345 HPFCI36	336 859		Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
			Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
				example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to

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measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
 can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,
 activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
pathways and alterations in cell functions.	stroke, and other diseases and disorders as described in the
Exemplary assays that may be used or	"Cardiovascular Disorders" section below), dyslipidemia,
 routinely modified to measure calcium flux	endocrine disorders (as described in the "Endocrine
by polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
Satin LS, et al., Endocrinology,	diseases and disorders as described in the "Infectious
136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
al., Endocrinology, 136(7):2960-6 (1995);	skin), carpal tunnel syndrome and Dupuytren's
Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
Cell Calcium 1989 Nov-Dec;10(8):535-41	obesity. Additional highly preferred indications include
(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
herein incorporated by reference in its	highly preferred indications are complications associated
entirety. Pancreatic cells that may be used	with insulin resistance.
according to these assays are publicly	
available (e.g., through the ATCC) and/or	
may be routinely generated. Exemplary	
pancreatic cells that may be used	
according to these assays include HITT15	
Cells. HITT15 are an adherent epithelial	
cell line established from Syrian hamster	
islet cells transformed with SV40. These	
cells express glucagon, somatostatin, and	
glucocorticoid receptors. The cells secrete	
insulin, which is stimulated by glucose and	
glucagon and suppressed by somatostatin	
or glucocorticoids. ATTC# CRL-1777	
Refs: Lord and Ashcroft. Biochem. J. 219:	
547-551; Santerre et al. Proc. Natl. Acad.	
Sci. USA 78: 4339-4343, 1981.	

					stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion,
					drowsiness, nonketotic hyperglycemic-hyperosmolar
					coma, cardiovascular disease (e.g., neart disease, atherosclerosis, microvascular disease, hypertension,
					stroke, and other diseases and disorders as described in the
					"Cardiovascular Disorders" section below), dyslipidemia,
					endocrine disorders (as described in the "Endocrine
					Disorders" section below), neuropathy, vision impairment
					(e.g., diabetic retinopathy and blindness), ulcers and
					impaired wound healing, infections (e.g., infectious
					diseases and disorders as described in the "Infectious
					Diseases" section below, especially of the urinary tract and
					skin), carpal tunnel syndrome and Dupuytren's
					contracture). An additional highly preferred indication
					is obesity and/or complications associated with obesity.
					Additional highly preferred indications include weight loss
					or alternatively, weight gain. Additional highly
					plication
					insulin resistance. Additional highly preferred
					indications are disorders of the musculoskeletal system
					including myopathies, muscular dystrophy, and/or as
					described herein. Additional highly preferred
					indications include: myopathy, atrophy, congestive heart
					failure, cachexia, myxomas, fibromas, congenital
					cardiovascular abnormalities, heart disease, cardiac arrest,
					heart valve disease, and vascular disease. Highly
					preferred indications include neoplasms and cancer, such
					as, rhabdomyoma, rhabdosarcoma, stomach, esophageal,
					prostate, and urinary cancer. Preferred indications also
					include breast, lung, colon, pancreatic, brain, and liver
	•				cancer. Other preferred indications include benign
					dysproliferative disorders and pre-neoplastic conditions,
					such as, hyperplasia, metaplasia, and/or dysplasia.
346	HPFDI37	098	Regulation of apoptosis in pancreatic beta cells.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication
				may be used or routinely modified to	associated with diabetes (e.g., diabetic retinopathy,

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	Series and the series are the series and the series and the series and the series are the series and the series and the series are the series and the series and the series are the series and the series are the series	
	assess the ability of polypeptides of the	diabetic nephropathy, kidney disease (e.g., renal failure,
	invention (including antibodies and	nephropathy and/or other diseases and disorders as
	agonists or antagonists of the invention) to	described in the "Renal Disorders" section below), diabetic
	promote caspase protease-mediated	neuropathy, nerve disease and nerve damage (e.g., due to
	apoptosis. Apoptosis in pancreatic beta is	diabetic neuropathy), blood vessel blockage, heart disease,
	associated with induction and progression	stroke, impotence (e.g., due to diabetic neuropathy or
	of diabetes. Exemplary assays for	blood vessel blockage), seizures, mental confusion,
	caspase apoptosis that may be used or	drowsiness, nonketotic hyperglycemic-hyperosmolar
	routinely modified to test capase apoptosis	coma, cardiovascular disease (e.g., heart disease,
	activity of polypeptides of the invention	atherosclerosis, microvascular disease, hypertension,
	(including antibodies and agonists or	stroke, and other diseases and disorders as described in the
	antagonists of the invention) include the	"Cardiovascular Disorders" section below), dyslipidemia,
	assays disclosed in: Loweth, AC, et al.,	endocrine disorders (as described in the "Endocrine
	FEBS Lett, 400(3):285-8 (1997); Saini,	Disorders" section below), neuropathy, vision impairment
	KS, et al., Biochem Mol Biol Int,	(e.g., diabetic retinopathy and blindness), ulcers and
	39(6):1229-36 (1996); Krautheim, A., et	impaired wound healing, and infection (e.g., infectious
	al., Br J Pharmacol, 129(4):687-94 (2000);	diseases and disorders as described in the "Infectious
	Chandra J, et al., Diabetes, 50 Suppl	Diseases" section below, especially of the urinary tract and
	1:S44-7 (2001); Suk K, et al., J Immunol,	skin), carpal tunnel syndrome and Dupuytren's
	166(7):4481-9 (2001); Tejedo J, et al.,	contracture). An additional highly preferred
	FEBS Lett, 459(2):238-43 (1999); Zhang,	indication is obesity and/or complications associated with
	S., et al., FEBS Lett, 455(3):315-20	obesity. Additional highly preferred indications include
	(1999); Lee et al., FEBS Lett 485(2-3):	weight loss or alternatively, weight gain. Aditional
•••	122-126 (2000); Nor et al., J Vasc Res	highly preferred indications are complications associated
	37(3): 209-218 (2000); and Karsan and	with insulin resistance.
	Harlan, J Atheroscler Thromb 3(2): 75-80	
	(1996); the contents of each of which are	
	herein incorporated by reference in its	
	entirety. Pancreatic cells that may be used	
	according to these assays are publicly	
	available (e.g., through the ATCC) and/or	
	may be routinely generated. Exemplary	
	pancreatic cells that may be used	
	according to these assays include RIN-m.	
	RIN-m is a rat adherent pancreatic beta	
	cell insulinoma cell line derived from a	
	radiation induced transplantable rat islet	

			cell tumor. The cells produce and secrete islet polypeptide hormones, and produce insulin, somatostatin, and possibly glucagon. ATTC: #CRL-2057 Chick et al. Proc. Natl. Acad. Sci. 1977 74:628; AF et al. Proc. Natl. Acad. Sci. 1980 77:3519.	
347	HPIAA80	Activation of Adipocyte ERK Signaling Pathway	kinase assays, for example kinase assay, for ERK signal tion that regulate cell proliferation artiation are well known in the art be used or routinely modified to e ability of polypeptides of the n' (including antibodies and or antagonists of the invention) to or inhibit cell proliferation. Exemplary or ERK kinase activity that may be outinely modified to test ERK iduced activity of polypeptides of tion (including antibodies and or antagonists of the invention) he assays disclosed in Forrer et Chem 379(8-9):1101-1110 Le Marchand-Brustel Y, Exp Clin nol Diabetes 107(2):126-132 Kyriakis JM, Biochem Soc Symp 8 (1999); Chang and Karin, Nature 4):37-40 (2001); and Cobb MH, phys Mol Biol 71(3-4):479-500 He contents of each of which are corporated by reference in its Mouse adipocyte cells that may according to these assays are available (e.g., through the	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., as described below under "Endocrine Disorders"). Highly preferred indications include endocrine disorders (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders", immune Activity", neural disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An

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include 3T3-L1 cells. 3T3-L1 is an associated with diabetes (e.g., diabetic retinopathy, adherent mouse preadipocyte cell line that	 	blood vessel blockage), seizures, mental confusion,	drowsiness, nonketotic nypergiycemic-nyperosmolar coma, cardiovascular disease (e.g., heart disease,	atherosclerosis, microvascular disease, hypertension,	stroke, and other diseases and disorders as described in the	"Cardiovascular Disorders" section below), dyslipidemia,	Endocrine disorders (as described in the Endocrine Disorders' section helow) neuropathy vision impairment	(e.g., diabetic retinopathy and blindness), ulcers and	impaired wound healing, infection (e.g., infectious	diseases and disorders as described in the "Infectious	Diseases" section below (particularly of the urinary tract	and skin). An additional highly preferred indication is	obesity and/or complications associated with obesity.	ndicat	Or alternatively, weight gain. Additional highly	preferred indications are complications associated with insulin resistance. Additional highly preferred	orders	including myopathies, muscular dystrophy, and/or as	described herein. Additional highly preferred	indications include, hypertension, coronary artery disease,	dyslipidemia, gallstones, osteoarthritis, degenerative	arthritis, eating disorders, fibrosis, cachexia, and kidney	diseases or disorders. Preferred indications include	neoplasms and cancer, such as, lymphoma, leukemia and	breast, colon, and kidney cancer. Additional preferred	indications include melanoma, prostate, lung, pancreatic,	esophageal, stomach, brain, liver, and urinary cancer.
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					liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
347	HPIAA80	861	Regulation of transcription of Malic Enzyme in adipocytes	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesis. Malic enzyme is stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as putative PPAR response elements. ME promoter may also responds to AP1 and other transcription factors. Exemplary assays that may be used or routinely modified to test for regulation of transcription of Malic Enzyme (in adipoocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Streeper, R.S., et al., Mol Endocrinol, 12(11):1778-91 (1998); Garcia-Jimenez, C., et al., Mol Endocrinol, 8(10):1361-9 (1994); Barroso, I., et al., J Biol Chem, 272(32):20108-20117 (1997); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362-368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic rephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Spisases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with insulin resistance. Additional highly preferred indications associated with insulin resistance.

				according to these assays are publicly available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				hepatocytes that may be used according to	
				these assays includes the H4IIE rat liver	
				hepatoma cell line.	
348	HPJBJ51	862	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
		•		participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
				cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
				Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
				differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
				a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
				expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
		-		modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.

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				include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-	Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodekin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	ΞĔ
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
349	HPJBJ51	863	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
				and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
				participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
				and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
				role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
			······································	cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
				of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
				disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
				chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
		•		Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
				differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
				a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
				expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
				cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
				are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
				or routinely modified to assess the ability	preferred indications also include boosting a B cell-
		•		of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate 1 cell proliferation and function.	asthma and allergy. Highly preferred indications include

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				Exemplary assays that test for	neonlastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia. lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
320	HPJBU43	864	Upregulation of CD152	CD152 FMAT. CD152 (a.k.a. CTLA-4)	A highly preferred embodiment of the invention
			and activation of T cells	expression is restricted to activated T cells.	includes a method for activating T cells. An alternative
				CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
				proliferation. Reduced CD152 expression	method for inhibiting the activation of and/or inactivating
				has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the
		4		autoimmune diseases. Overexpression of	invention includes a method for inhibiting T cell
		**************************************		CD152 may lead to impaired	proliferation. An alternative highly preferred embodiment
				immunoresponses. Assays for	of the invention includes a method for stimulating T cell
				immunomodulatory proteins important in	proliferation. Highly preferred indications include
				the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
	i L			expressed almost exclusively on CD4+ and	Activity", "Blood-Related Disorders", and/or

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Other preferred indications include benign dysproliferative 'Cardiovascular Disorders"), Highly preferred indications below), boosting a T cell-mediated immune response, and systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described eukopenia, thrombocytopenia, Hodgkin's disease, acute reactions to transplanted organs and tissues, hemophilia, include autoimmune diseases (e.g., rheumatoid arthritis, Highly preferred indications include neoplastic diseases melanoma, and prostate, breast, lung, colon, pancreatic, An (e.g., leukemia, lymphoma, and/or as described below ymphocytic anemia (ALL), plasmacytomas, multiple esophageal, stomach, brain, liver and urinary cancer. under "Hyperproliferative Disorders"). Additionally, disorders and pre-neoplastic conditions, such as, for granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune cancers, such as, for example, leukemia, lymphoma, Preferred indications include anemia, pancytopenia, highly preferred indications include neoplasms and example, hyperplasia, metaplasia, and/or dysplasia. additional preferred indication is infection (e.g., as hypercoagulation, diabetes mellitus, endocarditis, inflammatory disorders, and asthma and allergy. suppressing a T cell-mediated immune response. myeloma, Burkitt's lymphoma, arthritis, AIDS, meningitis, Lyme Disease, inflammation and described below under "Infectious Disease"). CD8+ T cells are well known in the art and otherwise known in the art. Human T cells agonists or antagonists of the invention) to et al., J Biomolecular Screening 4:193-204 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and upregulation of cell surface markers, such are herein incorporated by reference in its mature in the thymus and express a T Cell Such assays that may be used or routinely example, the assays disclosed in Miraglia 321 (1998), the contents of each of which entirety. Human T cells that may be used according to these assays may be isolated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the (2000); McCoy et al., Immunol Cell Biol antagonists of the invention) include, for (1999); Rowland et al., "Lymphocytes: a receptor and CD3, CD4, or CD8. These activity of polypeptides of the invention practical approach" Chapter 6:138-160 as CD152, and the activation of T cells. Saito T, Curr Opin Immunol 10(3):313assess the ability of polypeptides of the cells mediate humoral or cell-mediated including antibodies and agonists or immunity and may be preactivated to may be used or routinely modified to using techniques disclosed herein or are primary human lymphocytes that modified to test immunomodulatory invention (including antibodies and maintain T cell homeostasis, and/or modulate the activation of T cells, mediate humoral or cell-mediated enhance responsiveness to

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				immunomodulatory factors.	
350	HPJBU43	864	Upregulation of CD69	CD69 FMAT. CD69 is an activation	A highly preferred embodiment of the invention
			and activation of T cells	marker that is expressed on activated T	includes a method for activating T cells. An alternative
		· · · · · ·		cells, B cells, and NK cells. CD69 is not	highly preferred embodiment of the invention includes a
				expressed on resting T cells, B cells, or	method for inhibiting the activation of and/or inactivating
				NK cells. CD69 has been found to be	T cells. A highly preferred embodiment of the
				associated with inflammation. Assays for	invention includes a method for activation B cells. An
				immunomodulatory proteins expressed in	alternative highly preferred embodiment of the invention
		· ,		T cells, B cells, and leukocytes are well	
				known in the art and may be used or	inactivating B cells. A highly preferred embodiment
				routinely modified to assess the ability of	of the invention includes a method for activating NK cells.
				polypeptides of the invention (including	An alternative highly preferred embodiment of the
				antibodies and agonists or antagonists of	invention includes a method for inhibiting activation of
				the invention) to modulate the activation of	and/or inactivation NK cells. Highly preferred
				T cells, and/or mediate humoral or cell-	indications include inflammation and inflammatory
				mediated immunity. Exemplary assays	ė;
				that test for immunomodulatory proteins	Activity"). Preferred indications include blood
				evaluate the upregulation of cell surface	disorders (e.g., as described below under "Immune
				markers, such as CD69, and the activation	Activity", "Blood-Related Disorders", and/or
				of T cells. Such assays that may be used	"Cardiovascular Disorders"). Highly preferred indications
				or routinely modified to test	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory activity of	systemic lupus erythematosis, multiple sclerosis and/or as
				polypeptides of the invention (including	described below), immunodeficiencies (e.g., as described
				antibodies and agonists or antagonists of	below), boosting a T cell-mediated immune response and
				the invention) include, for example, the	alternatively suppressing a T cell-mediated immune
				assays disclosed in Miraglia et al., J	response, and boosting a B cell-mediated immune
				Biomolecular Screening 4:193-204 (1999);	response and alternatively suppressing a B cell-mediated
				Rowland et al., "Lymphocytes: a practical	immune response. An additional highly preferred
				approach" Chapter 6:138-160 (2000);	indication includes infection (e.g., as described below
				Ferenczi et al., J Autoimmun 14(1):63-78	under "Infectious Disease"). Preferred indications also
				(200); Werfel et al., Allergy 52(4):465-469	include anemia, pancytopenia, leukopenia,
			-	(1997); Taylor-Fishwick and Siegel, Eur J	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				Immunol 25(12):3215-3221 (1995); and	anemia (ALL), plasmacytomas, multiple myeloma,
				Afetra et al., Ann Rheum Dis 52(6):457-	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				460 (1993), the contents of each of which	disease, inflammatory bowel disease, sepsis, neutropenia,
				are herein incorporated by reference in its	neutrophilia, psoriasis, suppression of immune reactions to
				entirety. Human I cells that may be used	transplanted organs and tissues, nemophilia,

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351 HPJCW58 865 Regulation of A transcription through the the FAS promoter we element in hepatocytes read a a a a a a a a a a a a a a a a a a	receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
	Assays for the regulation of transcription through the FAS promoter element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the FAS promoter element in a reporter construct and to regulate transcription of FAS, a key enzyme for lipogenesis. FAS promoter is regulated by many transcription factors including SREBP. Insulin increases FAS gene transcription in livers of diabetic mice. This stimulation of transcription is also somewhat glucose dependent. Exemplary assays that may be used or routinely modified to test for FAS promoter element activity (in hepatocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Xiong, S., et al., Proc Natl Acad Sci U.S.A., 97(8):3948-53 (2000); Roder, K., et al., Eur J Biochem, 260(3):743-51	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetes (e.g., diabetic retinopathy, diabetes (e.g., diabetic retinopathy, nerve diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with

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HPMBX22 8	866	Production of IL-6	(Pt 1):257-65 (1996); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these assays, such as H4IIE cells, are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays include rat liver hepatoma cell line(s) inducible with glucocorticoids, insulin, or cAMP derivatives. IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention and differentiation and differentiation.	weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cellmediated immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred indicational highly preferred indications include inflammation and inflammatory disorders. Additional highly preferred indications include inflammation and inflammatory
			modulate T cell proliteration and function. Exemplary assays that test for imminoration and instance the	asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma, larkemin lymphoms melonoms and on a described

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				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
353	HPMCJ84	<i>L</i> 98	Activation of	Assays for the activation of transcription	A highly preferred embodiment of the invention
			transcription through	through the CD28 response element are	includes a method for stimulating T cell proliferation. An
			CD28 response element	well-known in the art and may be used or	alternative highly preferred embodiment of the invention
			in immune cells (such	routinely modified to assess the ability of	includes a method for inhibiting T cell proliferation.
			as T-cells).	polypeptides of the invention (including	highly preferred embodiment of the invention includes a
				antibodies and agonists or antagonists of	method for activating T cells. An alternative highly
				the invention) to stimulate IL-2 expression	preferred embodiment of the invention includes a method
				in T cells. Exemplary assays for	for inhibiting the activation of and/or inactivating T cells.
				transcription through the CD28 response	A highly preferred embodiment of the invention includes a
				element that may be used or routinely	method for stimulating (e.g., increasing) IL-2 production.
				modified to test CD28-response element	An alternative highly preferred embodiment of the
				activity of polypeptides of the invention	s a r
				(including antibodies and agonists or	IL-2 production. Additional highly preferred

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antagonists of the invention) include	disorders Utiebly preferred indications include
66:1-10 (1998); Cullen and Malm,	စ္
Methods in Enzymol 216:362-368 (1992);	lupus erythematosis, multiple sclerosis and/or as described
Henthorn et al., Proc Natl Acad Sci USA	below), immunodeficiencies (e.g., as described below),
85:6342-6346 (1988); McGuire and	boosting a T cell-mediated immune response, and
Iacobelli, J Immunol 159(3):1319-1327	suppressing a T cell-mediated immune response. An
(1997); Parra et al., J Immunol	additional highly preferred indication includes infection
166(4):2437-2443 (2001); and Butscher et	(e.g., AIDS, and/or as described below under "Infectious
al., J Biol Chem 3(1):552-560 (1998), the	Disease"). Highly preferred indications include
contents of each of which are herein	neoplastic diseases (e.g., melanoma, renal cell carcinoma,
incorporated by reference in its entirety. T	leukemia, lymphoma, and/or as described below under
cells that may be used according to these	"Hyperproliferative Disorders"). Highly preferred
assays are publicly available (e.g., through	indications include neoplasms and cancers, such as, for
the ATCC). Exemplary human T cells that	example, melanoma (e.g., metastatic melanoma), renal cell
may be used according to these assays	carcinoma (e.g., metastatic renal cell carcinoma),
include the JURKAT cell line, which is a	leukemia, lymphoma (e.g., T cell lymphoma), and
suspension culture of leukemia cells that	prostate, breast, lung, colon, pancreatic, esophageal,
produce IL-2 when stimulated.	stomach, brain, liver and urinary cancer. Other preferred
	indications include benign dysproliferative disorders and
	pre-neoplastic conditions, such as, for example,
	hyperplasia, metaplasia, and/or dysplasia. A highly
	preferred indication is infection (e.g., tuberculosis,
	infections associated with granulomatous disease, and
	osteoporosis, and/or an infectious disease as described
	below under "Infectious Disease"). A highly preferred
	indication is AIDS. Additional highly preferred
	indications include suppression of immune reactions to
	transplanted organs and/or tissues, uveitis, psoriasis, and
	tropical spastic paraparesis. Preferred indications
	include blood disorders (e.g., as described below under
	"Immune Activity", "Blood-Related Disorders", and/or
	"Cardiovascular Disorders"). Preferred indications also
	include anemia, pancytopenia, leukopenia,
	thrombocytopenia, Hodgkin's disease, acute lymphocytic
	anemia (ALL), plasmacytomas, multiple myeloma,
	Burkitt's lymphoma, arthritis, granulomatous disease,

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354	HPMCV30	. 898	Production of ICAM-1	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly	inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy. Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
355	HPMFH77	698	Activation of transcription through serum response element in immune cells (such as T-cells).	available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC). Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated

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			activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
			invention (including antibodies and	immune response. Additional highly preferred indications
			agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
			include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
			Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
			Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
			Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
			85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
			Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
			content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
			incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
			cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
			assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
			the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
			may be used according to these assays	pre-neoplastic conditions, such as, for example,
			include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
			2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
		-	with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				anemia (ALL), plasmacytomas, multiple myeloma,
				Burkitt's lymphoma, arthritis, AIDS, granulomatous
				disease, inflammatory bowel disease, neutropenia,
				neutrophilia, psoriasis, suppression of immune reactions to
				transplanted organs and tissues, hemophilia,
				hypercoagulation, diabetes mellitus, endocarditis,
				meningitis, Lyme Disease, cardiac reperfusion injury, and
				asthma and allergy. An additional preferred indication
				is infection (e.g., an infectious disease as described below
\pm				under "Infectious Disease").
356 HPQAX38	870	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
		transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
		serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
		in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
		as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
			(including antibodies and agonists or	include blood disorders (e.g., as described below under
			antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
			the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
			the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,

				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
	-			transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
		,		the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
357	HPQAX38	871	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under

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				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
358	HPQCB83	872	Activation of Endothelial Cell p38 or	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth.
			JNK Signaling	proliferation, activation, or apoptosis are	An alternative highly preferred embodiment of the

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Pathway.	well known in the art and may be used or	invention includes a method for inhibiting endothelial cell
•	routinely modified to assess the ability of	growth. A highly preferred embodiment of the
	polypeptides of the invention (including	invention includes a method for stimulating endothelial
	antibodies and agonists or antagonists of	cell proliferation. An alternative highly preferred
	the invention) to promote or inhibit cell	embodiment of the invention includes a method for
	proliferation, activation, and apoptosis.	inhibiting endothelial cell proliferation. A highly
	Exemplary assays for JNK and p38 kinase	preferred embodiment of the invention includes a method
	activity that may be used or routinely	for stimulating apoptosis of endothelial cells. An
	modified to test JNK and p38 kinase-	alternative highly preferred embodiment of the invention
	induced activity of polypeptides of the	includes a method for inhibiting (e.g., decreasing)
	invention (including antibodies and	apoptosis of endothelial cells. A highly preferred
	agonists or antagonists of the invention)	embodiment of the invention includes a method for
***	include the assays disclosed in Forrer et	stimulating (e.g., increasing) endothelial cell activation.
	al., Biol Chem 379(8-9):1101-1110	An alternative highly preferred embodiment of the
	(1998); Gupta et al., Exp Cell Res 247(2):	invention includes a method for inhibiting (e.g.,
	495-504 (1999); Kyriakis JM, Biochem	decreasing) the activation of and/or inactivating
	Soc Symp 64:29-48 (1999); Chang and	endothelial cells. A highly preferred embodiment of
	Karin, Nature 410(6824):37-40 (2001);	the invention includes a method for stimulating
	and Cobb MH, Prog Biophys Mol Biol	angiogenisis. An alternative highly preferred embodiment
	71(3-4):479-500 (1999); the contents of	of the invention includes a method for inhibiting
	each of which are herein incorporated by	angiogenesis. A highly preferred embodiment of the
 	reference in its entirety. Endothelial cells	invention includes a method for reducing cardiac
	that may be used according to these assays	hypertrophy. An alternative highly preferred embodiment
	are publicly available (e.g., through the	of the invention includes a method for inducing cardiac
	ATCC). Exemplary endothelial cells that	hypertrophy. Highly preferred indications include
	may be used according to these assays	neoplastic diseases (e.g., as described below under
	include human umbilical vein endothelial	"Hyperproliferative Disorders"), and disorders of the
	cells (HUVEC), which are endothelial	cardiovascular system (e.g., heart disease, congestive heart
	cells which line venous blood vessels, and	failure, hypertension, aortic stenosis, cardiomyopathy,
	are involved in functions that include, but	valvular regurgitation, left ventricular dysfunction,
	are not limited to, angiogenesis, vascular	atherosclerosis and atherosclerotic vascular disease,
	permeability, vascular tone, and immune	diabetic nephropathy, intracardiac shunt, cardiac
	cell extravasation.	hypertrophy, myocardial infarction, chronic hemodynamic
		overload, and/or as described below under
		"Cardiovascular Disorders"). Highly preferred indications
		include cardiovascular, endothelial and/or angiogenic
		disorders (e.g., systemic disorders that affect vessels such

as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins and/or	lymphatics). Highly preferred are indications that	stimulate angiogenesis and/or cardiovascularization.	Highly preferred are indications that inhibit angiogenesis	and/or cardiovascularization. Highly preferred	indications include antiangiogenic activity to treat solid	tumors, leukemias, and Kaposi's sarcoma, and retinal	disorders. Highly preferred indications include neoplasms	and cancer, such as, Kaposi's sarcoma, hemangioma	(capillary and cavernous), glomus tumors, telangiectasia,	bacillary angiomatosis, hemangioendothelioma,	angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver, and urinary	cancer. Preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions,	such as, for example, hyperplasia, metaplasia, and/or	dysplasia. Highly preferred indications also include	arterial disease, such as, atherosclerosis, hypertension,	coronary artery disease, inflammatory vasculitides,	Reynaud's disease and Reynaud's phenomenom,	aneurysms, restenosis; venous and lymphatic disorders	such as thrombophiebitis, lymphangitis, and lymphedema;	and other vascular disorders such as peripheral vascular	disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue	(e.g., vascular injury such as, injury resulting from balloon	angioplasty, and atheroschlerotic lesions), implant	fixation, scarring, ischemia reperfusion injury, rheumatoid	arthritis, cerebrovascular disease, renal diseases such as	acute renal failure, and osteoporosis. Additional highly	preferred indications include stroke, graft rejection,	diabetic or other retinopathies, thrombotic and coagulative	disorders, vascularitis, lymph angiogenesis, sexual	disorders, age-related macular degeneration, and treatment
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			·		Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below). Additional preferred indications include inflammation and inflammatory diseases, e.g., inflammatory bowel disease
359 F	HPQCC53	873	Production of MCP-1	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation. Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as monocyte chemoattractant protein (MCP), and the activation of monocytes and T cells. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or protein to including antibodies and agonists or protein in the activation of the invention (including antibodies and agonists or protein to the production of the invention (including antibodies and agonists or protein the production of the invention (including antibodies and agonists or protein the production of the invention (including antibodies and agonists or protein the production of the invention (including antibodies and agonists or protein the production of the invention (including antibodies and agonists or protein the production of the invention (including antibodies and agonists).	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs

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360 HPRBH85 874	Stimulation of insulin secretion from pancreatic beta cells.	assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by	mellitus, endocarditis, meningitis (bacterial and viral), Lyme Disease, asthma, and allergy Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below, diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizuures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine
		polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in:	Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious

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				Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al.	diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
361	HPRCA64	875	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention)	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as

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include the assays disclosed in Foal, Biol Chem 379(8-9):1101-1111 (1998); Le Marchand-Brustel Y, Endocrinol Diabetes 107(2):126-1 (1999); Kyriskis JM, Biochem So 64:29-48 (1999); Chang and Karit 410(6824):37-40 (2001); and Cob Prog Biophys Mol Biol 71(3-4):4 (1999); the contents of each of wherein incorporated by reference i entirely. Mouse adipocyte cells the be used according to these assays publicily available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these include 3T3-L1 (ells. 3T3-L1) is a adherent mouse preadipocyte cell is a continuous abstrain of 3T3 fit cells developed through clonal iso and undergo a preadipocyte to ad like conversion under appropriate differentiation conditions known it	al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.	beld in the control of the control o	
		and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss	

					or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or
362	HPRCD35	876	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux by polypeptides of the invention (including antibodies and agonists or antagonists of	A highly preferred indication is diabetes mellitus. A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment fer or diabetic retinorathy and blindness), pleers and

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				quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
				signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
				active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
				used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
				regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
				pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
				invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
				agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
		-		include assays disclosed in: Ohtani KI, et	diseases and disorders as described in the "Infectious
				al., Endocrinology, 139(1):172-8 (1998);	Diseases" section below, especially of the urinary tract and
				Krautheim A, et al, Exp Clin Endocrinol	skin), carpal tunnel syndrome and Dupuytren's
				Diabetes, 107 (1):29-34 (1999), the	contracture). An additional highly preferred
				contents of each of which is herein	indication is obesity and/or complications associated with
				incorporated by reference in its entirety.	cations i
				Pancreatic cells that may be used	weight loss or alternatively, weight gain. Aditional
				according to these assays are publicly	highly preferred indications are complications associated
				available (e.g., through the ATCC) and/or	with insulin resistance.
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include HITT15	
				Cells. HITT15 are an adherent epithelial	
				cell line established from Syrian hamster	
				islet cells transformed with SV40. These	
				cells express glucagon, somatostatin, and	
				glucocorticoid receptors. The cells secrete	
				insulin, which is stimulated by glucose and	
				glucagon and suppressed by somatostatin	
				or glucocorticoids. ATTC# CRL-1777	
				Refs: Lord and Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc. Natl. Acad.	
				Sci. USA 78: 4339-4343, 1981.	
363	HPTRM02	877	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt s lympnoma, non-Hodgkins lympnoma, Hodgkins

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				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
			-	transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
				may be used according to these assays are	include anemia, pancytopenia, leukopenia,
				publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
				ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
				used according to these assays include the	granulomatous disease, inflammatory bowel disease,
				CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
				cells.	hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
364	HPWBA29	878	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
			transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
			NFAT response in	cells (NFAT) response element are well-	"Blood-Related Disorders", and/or "Cardiovascular
			immune cells (such as	known in the art and may be used or	Disorders"). Highly preferred indications include
			T-cells).	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				polypeptides of the invention (including	lupus erythematosis, multiple sclerosis and/or as described
				antibodies and agonists or antagonists of	below), immunodeficiencies (e.g., as described below),

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				the invention) to regulate NFAT	boosting a T cell-mediated immune response, and
				transcription factors and modulate	suppressing a T cell-mediated immune response.
				expression of genes involved in	Additional highly preferred indications include
				immunomodulatory functions. Exemplary	inflammation and inflammatory disorders. An additional
				assays for transcription through the NFAT	highly preferred indication is infection (e.g., an infectious
				response element that may be used or	disease as described below under "Infectious Disease").
				routinely modified to test NFAT-response	Preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
				agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
				include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
				Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
				Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
				Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
				85:6342-6346 (1988); Serfling et al.,	such as, for example, hyperplasia, metaplasia, and/or
				Biochim Biophys Acta 1498(1):1-18	dysplasia. Preferred indications also include anemia,
				(2000); De Boer et al., Int J Biochem Cell	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				Biol 31(10):1221-1236 (1999); Fraser et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., Eur J Immunol 29(3):838-844 (1999);	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				and Yeseen et al., J Biol Chem	granulomatous disease, inflammatory bowel disease,
				268(19):14285-14293 (1993), the contents	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				of each of which are herein incorporated	immune reactions to transplanted organs and tissues,
				by reference in its entirety. T cells that	hemophilia, hypercoagulation, diabetes mellitus,
				may be used according to these assays are	endocarditis, meningitis, Lyme Disease, asthma and
				publicly available (e.g., through the	allergy.
	,			ATCC). Exemplary human T cells that	
				may be used according to these assays	
				include the JURKAT cell line, which is a	
				suspension culture of leukemia cells that	
				produce IL-2 when stimulated.	
364	HPWBA29	878	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,

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HPWDK06 879 Upregulation of 0	the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4 cell line, that may be used according to these assays are publicly available (e.g., through the ATCC). CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells proliferation. Reduced CD152 expression has been linked to hyperproliferative and has been linked to hyperproliferative and has been linked to hyperproliferative and	pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), immunodeficiencies (e.g., as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include blood disorders. Highly preferred indications infections, tuberculosis, infections associated with chronic granulomatory disorders (e.g., as described below under "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatous disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells.
	CD152 may lead to impaired	proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating T cell

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"Cardiovascular Disorders"), Highly preferred indications Other preferred indications include benign dysproliferative below), boosting a T cell-mediated immune response, and systemic lupus erythematosis, multiple sclerosis and/or as blood disorders (e.g., as described below under "Immune described below), immunodeficiencies (e.g., as described eukopenia, thrombocytopenia, Hodgkin's disease, acute include autoimmune diseases (e.g., rheumatoid arthritis, reactions to transplanted organs and tissues, hemophilia, Highly preferred indications include neoplastic diseases melanoma, and prostate, breast, lung, colon, pancreatic, Highly preferred indications include (e.g., leukemia, lymphoma, and/or as described below lymphocytic anemia (ALL), plasmacytomas, multiple esophageal, stomach, brain, liver and urinary cancer. under "Hyperproliferative Disorders"). Additionally, disorders and pre-neoplastic conditions, such as, for granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune cancers, such as, for example, leukemia, lymphoma, Preferred indications include anemia, pancytopenia, highly preferred indications include neoplasms and example, hyperplasia, metaplasia, and/or dysplasia. additional preferred indication is infection (e.g., as hypercoagulation, diabetes mellitus, endocarditis, suppressing a T cell-mediated immune response. inflammatory disorders, and asthma and allergy. myeloma, Burkitt's lymphoma, arthritis, AIDS, Activity", "Blood-Related Disorders", and/or meningitis, Lyme Disease, inflammation and described below under "Infectious Disease"). proliferation. expressed almost exclusively on CD4+ and CD8+ T cells are well known in the art and otherwise known in the art. Human T cells agonists or antagonists of the invention) to the maintenance of T cell homeostasis and et al., J Biomolecular Screening 4:193-204 77(1):1-10 (1999); Oostervegal et al., Curr mmunomodulatory proteins important in upregulation of cell surface markers, such Opin Immunol 11(3):294-300 (1999); and are herein incorporated by reference in its example, the assays disclosed in Miraglia immunity. Exemplary assays that test for immunomodulatory proteins evaluate the Such assays that may be used or routinely 321 (1998), the contents of each of which entirety. Human T cells that may be used mature in the thymus and express a T Cell (1999); Rowland et al., "Lymphocytes: a according to these assays may be isolated (2000); McCoy et al., Immunol Cell Biol antagonists of the invention) include, for eceptor and CD3, CD4, or CD8. These activity of polypeptides of the invention practical approach" Chapter 6:138-160 Saito T, Curr Opin Immunol 10(3):313assess the ability of polypeptides of the as CD152, and the activation of T cells. may be used or routinely modified to including antibodies and agonists or using techniques disclosed herein or are primary human lymphocytes that modified to test immunomodulatory invention (including antibodies and maintain T cell homeostasis, and/or modulate the activation of T cells, mediate humoral or cell-mediated

				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
399	HRAAD30	880	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
				or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred
				agonists or antagonists of the invention) to	embodiment of the invention includes a method for
				promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
				activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
				assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
				used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
				kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
				the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
				agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
				include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
				al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
				(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
				Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
				(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
				64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
				410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
				Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
				(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
				herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
	•			entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
				be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
				publicly available (e.g., through the	described below under "Infectious Disease").
				ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
				that may be used according to these assays	additional highly preferred indication is a complication
				include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
				adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
				is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as

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cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.
	Additional highly preferred indications include weight loss
	or alternatively, weight gain. Additional highly
	preferred indications are complications associated with
	insulin resistance. Additional highly preferred
	indications are disorders of the musculoskeletal systems
	including myopathies, muscular dystrophy, and/or as
	described herein. Additional highly preferred
	indications include, hypertension, coronary artery disease,
	dyslipidemia, gallstones, osteoarthritis, degenerative
	arthritis, eating disorders, fibrosis, cachexia, and kidney
	diseases or disorders. Preferred indications include
	neoplasms and cancer, such as, lymphoma, leukemia and
	breast, colon, and kidney cancer. Additional preferred
	indications include melanoma, prostate, lung, pancreatic,
	esophageal, stomach, brain, liver, and urinary cancer.
	Highly preferred indications include lipomas and
	liposarcomas. Other preferred indications include benign
	dysproliferative disorders and pre-neoplastic conditions,
	such as, for example, hyperplasia, metaplasia, and/or

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367	HRADA42	881	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
		-		assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			. —		anemia (ALL), plasmacytomas, multiple myeloma,
٠					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,

			asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
368 HRADF49 882	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 373-L1 is an adherent mouse preadipocyte cell line that	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and Neurological Diseases"), and infection (e.g., as described below under "Infrantune Activity", and Neurological Diseases"). A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure,

cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
 differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.
	Additional highly preferred indications include weight loss
	or alternatively, weight gain. Additional highly
	preferred indications are complications associated with
	insulin resistance. Additional highly preferred
	indications are disorders of the musculoskeletal systems
	including myopathies, muscular dystrophy, and/or as
	described herein. Additional highly preferred
	indications include, hypertension, coronary artery disease,
	dyslipidemia, gallstones, osteoarthritis, degenerative
	arthritis, eating disorders, fibrosis, cachexia, and kidney
	diseases or disorders. Preferred indications include
	neoplasms and cancer, such as, lymphoma, leukemia and
	breast, colon, and kidney cancer. Additional preferred
	indications include melanoma, prostate, lung, pancreatic,
	esophageal, stomach, brain, liver, and urinary cancer.
	Highly preferred indications include lipomas and
	liposarcomas. Other preferred indications include benign
	dysproliferative disorders and pre-neoplastic conditions,
	such as, for example, hyperplasia, metaplasia, and/or

					dysplasia.
368	HRADF49	882	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
		_		used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
			. •	with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
			-		transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,

					meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below under "Infectious Disease").
369 F	HRADN25	883	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) INF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative pretented embodifficial of the
			in immune cells (such	be used or routinely modified to assess the	increasing) TNE slabs production Preferred indications
			as 1-cells).	donney of polypeptides of the invention (including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
		.,		the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,

				neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
370 HRADT25	888	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, immunodeficiency (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. Additional preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia,
			the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications

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include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, ontents meningitis, Lyme Disease, asthma and allergy. I cells assays closed USD4, al or ess to	referred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke ion) to plary ssion P, et al, d, nts of lby nay be ublicly
in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly
	Production of ICAM-1
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				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				cells that may be used according to these	
				assays include microvascular endothelial	
orounan 628	\dagger	988	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
		3	transcription via	through the DMFF1 response element are	An additional highly preferred indication is a complication
		_	DMEET response	well-known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			element in adinocytes	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
			and pre-adinocytes	polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
	-			antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to activate the DMEF1	neuropathy, nerve disease and nerve damage (e.g., due to
				response element in a reporter construct	diabetic neuropathy), blood vessel blockage, heart disease,
				(such as that containing the GLUT4	stroke, impotence (e.g., due to diabetic neuropathy or
				promoter) and to regulate insulin	blood vessel blockage), seizures, mental confusion,
				production. The DMEF1 response	drowsiness, nonketotic hyperglycemic-hyperosmolar
				element is present in the GLUT4 promoter	coma, cardiovascular disease (e.g., heart disease,
	•			and binds to MEF2 transcription factor and	atherosclerosis, microvascular disease, hypertension,
				another transcription factor that is required	stroke, and other diseases and disorders as described in the
				for insulin regulation of Glut4 expression	"Cardiovascular Disorders" section below), dyslipidemia,
				in skeletal muscle. GLUT4 is the primary	endocrine disorders (as described in the "Endocrine
,				insulin-responsive glucose transporter in	Disorders" section below), neuropathy, vision impairment
				fat and muscle tissue. Exemplary assays	(e.g., diabetic retinopathy and blindness), ulcers and
				that may be used or routinely modified to	impaired wound healing, and infection (e.g., infectious
				test for DMEF1 response element activity	diseases and disorders as described in the "Infectious
				(in adipocytes and pre-adipocytes) by	Diseases" section below, especially of the urinary tract and
				polypeptides of the invention (including	tunnel
				antibodies and agonists or antagonists of	contracture). An additional highly preferred
	-			the invention) include assays disclosed	indication is obesity and/or complications associated with
				inThai, M.V., et al., J Biol Chem,	ications i
				273(23):14285-92 (1998); Mora, S., et al.,	weight loss or alternatively, weight gain. Aditional
				J Biol Chem, 275(21):16323-8 (2000); Liu,	highly preferred indications are complications associated
				M.L., et al., J Biol Chem, 269(45):28514-	with insulin resistance.
				21 (1994); "Identification of a 30-base pair	
				regulatory element and novel DNA	
1				binding protein that regulates the human	
				GLUT4 promoter in transgenic mice", J	

Biol Chem. 2000 Aug 4;275(31):23666-73; Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Adipocytes and pre-adipocytes that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the mouse 3T3-L1 cell line which is an adherent mouse preadipocyte cell line. Mouse 3T3-L1 cells are a continuous substrain of 3T3 fibroblasts developed through clonal isolation. These cells undergo a pre-adipocyte to adipose-like conversion under appropriate	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the suragonists of resum response factors and agonists or the serum response factors and modulate expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be cativity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention). A preferred embodiment of the invention includes a method for stimulating (e.g., reducing) TNF alpha production. Preferred indications include below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, An additional highly preferred indication is sepsis. A preduction antibodies a method for stimulating (e.g., reducing) TNF alpha production. Preferred indications includes a method for stimulating (e.g., inventing) (e.g., includes a method for stimulating (e.g., including antibodies and modulate "Cardiovascular Disorders"), Highly preferred indications includes a method for stimulation (e.g., includes indication including antipodic (e.g., includes a method for stimulation (e.g., includes indication including antipodic (e.g., includes indication (e.g., includes indication (e.g., includes indication (e.
CHOCHECHECHECHECHECHECHECHECHECHECHECHECHEC	Activation of transcription through serum response element in immune cells (such as a sa T-cells).
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372 HRDDQ39 886	Stimulation of insulin secretion from pancreatic beta cells.	Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity. Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary	(e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitr's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is suffectious Disease, and disorders as associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy and/or other diseases and disorders as associated with diabetes (e.g., diabetic retinopathy or diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and eichyperension, athroscelerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the diseases, and disorders as described in the diseases and disorders as
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endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications associated with insulin resistance. S-1 S-1 i. C.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies
secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be
	Activation of transcription through serum response element in immune cells (such as T-cells).
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(e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infectiou Geg., an infectious disease as described below under "Infectious Disease").	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease,
used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	Assays for the regulation of transcription through the FAS promoter element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the FAS promoter element in a reporter construct
	Regulation of transcription through the FAS promoter element in hepatocytes
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erosmolar isease, bertension, described in the described in the indocrine sion impairment alcers and g., infectious urinary tract and en's eferred associated with ations include Aditional ons associated	n includes a F alpha d embodiment of ating (e.g., erred indications
blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications associated with insulin resistance.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described helow under
enzyme for lipogenesis. FAS promoter is regulated by many transcription factors including SREBP. Insulin increases FAS gene transcription in livers of diabetic mice. This stimulation of transcription is also somewhat glucose dependent. Exemplary assays that may be used or routinely modified to test for FAS promoter element activity (in hepatocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Xiong, S., et al., Proc Natl Acad Sci U.S.A., 97(8):3948-53 (2000); Roder, K., et al., Eur J Biochem, 260(3):743-51 (1999); Oskouian B, et al., Biochem J, 317 (Pt 1):257-65 (1996); Berger, et al., Gene 66:1-10 (1988); and, Cullen, B., et al., Methods in Enzymol. 216:362–368 (1992), the contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used according to these assays, such as H4IIE cells, are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays include rat liver hepatoma cell line(s) inducible with glucocorticoids, insulin, or cAMP derivatives.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention discluding antibodies and agonists or
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
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				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or	<u> </u>
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,	
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple	
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies	
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated	
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated	
				modified to test SRE activity of the	immune response. Additional highly preferred indications	
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and	
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.	
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.	
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases	
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below	
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,	
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and	
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,	_
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,	
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,	
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred	
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and	
				be used according to these assays are	pre-neoplastic conditions, such as, for example,	
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred	
				ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,	
				used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic	
				NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,	
				killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous	
				activity.	disease, inflammatory bowel disease, neutropenia,	
					neutrophilia, psoriasis, suppression of immune reactions to	
					uanspianted of gains and ussues, inclinopinia,	
					nypercoagulation, diabetes mellitus, endocardius,	
					meningitis, Lyme Disease, cardiac reperfusion injury, and	
					asthma and allergy. An additional preferred indication	
					is infection (e.g., an infectious disease as described below	
					under Infectious Disease).	Т
376	HRGBD54	068	Production of IFNgamma using a T	IFNgamma FMAT. IFNg plays a central role in the immune system and is	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg.	
			cells	considered to be a proinflammatory	An alternative highly preterred embodiment of the	\neg

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	cytokine. IFNg promotes TH1 and	inclu
	inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
	IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
	macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
	MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
	immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
	T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
	of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
	helper cell functions are well known in the	Highly preferred indications include autoimmune disease
	art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
	to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
-	invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
	agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
	mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
	inflammatory activities, modulate TH2	indications include inflammation and inflammatory
	helper cell function, and/or mediate	disorders. Additional preferred indications include
	humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
	Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
	immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
	production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
	gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
	cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
	routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
	immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
	polypeptides of the invention (including	include benign dysproliferative disorders and pre-
	antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
	the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
	in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
	Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
	al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
	Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
	J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
	Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
	(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
	15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
	Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
	of each of which are herein incorporated	

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			that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to	
377 HROEA08	891	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine Disorders (e.g., as described below under "Endocrine Disorders"). Highly preferred indications also include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), immune Activity"), neural

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assays ne that coblast tion ose- the art.	be used according to these assays are publicly available (e.g., through the	and Neurological Diseases"), and infection (e.g., as described below under "Infectious Disease").
	ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
tt st	that may be used according to these assays	additional highly preferred indication is a complication
is ti	include 313-L1 cells. 313-L1 is an adherent mouse preadinocyte cell line that	associated with diabetes (e.g., diabetic rethiopaury, diabetic nephropathy, kidney disease (e.g., renal failure.
<u>ដ</u>	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
ţ	cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
hlood vesse drowsiness, coma, cardi anterosclerra stroke, and "Cardiovass endocrine d Disorders" (e.g., diabel impaired w diseases and Diseases" s and skin). obesity and Additional or alternations indications including r described h indications dyslipidemi arthritis, ca	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
drowsiness, coma_cardi antosclerr stroke, and "Cardiovass endocrine d Disorders" (e.g., diabel impaired w diseases an diseases and skin), obesity and Additional or alternativ preferred in insulin resis indications discases or discases or		blood vessel blockage), seizures, mental confusion,
coma, cardi atherosclerc stroke, and "Cardiovasa endocrine d Disorders" (e.g., diabet impaired w diseases an Diseases an Diseases an diseases an diseases an destity and Additional or alternatiy preferred in insulin resis indications described h indications diseases or diseases or		drowsiness, nonketotic hyperglycemic-hyperosmolar
atherosclerc stroke, and "Cardiovass endocrine d Disorders" (e.g., diabel impaired w diseases and Diseases" s and skin). Obesity and Additional or alternative preferred in insulin resis indications indications dyslipidemi arthritis, ea diseases or disease		coma, cardiovascular disease (e.g., heart disease,
stroke, and "Cardiovasa endocrine d Disorders". (e.g., diabel impaired w diseases and diseases and skin). obesity and Additional or alternativ preferred in insulin resis indications indications diseases or		atherosclerosis, microvascular disease, hypertension,
"Cardiovass endocrine d Disorders" (e.g., diabel impaired wo diseases and Diseases and Diseases and Skin). Obesity and Additional or alternating preferred in insulin resis indications including reserving dyslipidemi arthritis, ea diseases or the disease or the diseases or the diseases or the disease or th		stroke, and other diseases and disorders as described in the
endocrine d Disorders" (e.g., diabet impaired w diseases an Diseases an Diseases, a and skin). obesity and Additional or alternatin preferred in insulin resis indications including r described h indications dyslipidemi arthritis, ea		"Cardiovascular Disorders" section below), dyslipidemia,
Disorders" (e.g., diabet impaired we diseases and Diseases" sand skin). Obesity and Additional or alternative preferred in insulin resis indications including meetrifications indications dyslipidemia arthritis, earthritis,		endocrine disorders (as described in the "Endocrine
(e.g., diabet impaired we diseases and Diseases" so and skin). Obesity and Additional or alternative preferred in insulin resis indications including mescribed he indications dyslipidemia arthritis, ea diseases or alternative control or alternative co	-	Disorders" section below), neuropathy, vision impairment
impaired working the diseases and diseases and Diseases" sand skin). Obesity and Additional or alternative preferred in insulin resis indications including received he indications dyslipidemi arthritis, ear diseases or disease or diseases or diseases or disease or		(e.g., diabetic retinopathy and blindness), ulcers and
diseases an Diseases" s and skin). obesity and Additional or alternative preferred in insulin resis indications including m described h indications dyshipidemi arthritis, ea diseases or alternative.		impaired wound healing, infection (e.g., infectious
Diseases" s and skin). obesity and Additional or alternativ preferred in insulin resis indications including m described h indications dyslipidem arthritis, ea		diseases and disorders as described in the "Infectious
and skin). obesity and Additional or alternative preferred in insulin resisive indications including madescribed here indications dyslipidemi arthritis, ear diseases or		sec
Additional Additional or alternativ preferred in insulin resis indications including m described h indications dyslipidemi arthritis, ea		and skin). An additional highly preferred indication is
Additional or alternation preferred in insulin resist indications including machine indications including machines indications dyslipidemi arthritis, ea disease or deserved the indications dyslipidemi arthritis, ea disease or deserved the indications diseases or deserved the indications dyslipidemi arthritis, ear diseases or deserved the indications disease or deserved the indications diseases disease		obesity and/or complications associated with obesity.
or alternation preferred in insulin resis indications including m described h indications dyslipidemi arthritis, ea disease or each of the contract of the con		ndicat
preferred in sulin resisions indications including mescribed hindications dyslipidemi arthritis, ea diseases or		or alternatively, weight gain. Additional highly
insulin resi indications including m described h indications dyslipidemi arthritis, ea diseases or		ns are
including m described h indications dyslipidemi arthritis, ea diseases or		insulin resistance. Additional highly preferred
including m described h indications dyslipidemi arthritis, ea diseases or		indications are disorders of the musculoskeletal systems
described h indications dyslipidemi arthritis, ea diseases or		including myopathies, muscular dystrophy, and/or as
indications dyslipidemi arthritis, ea diseases or		described herein. Additional highly preferred
dyslipidemi arthritis, ea diseases or		indications include, hypertension, coronary artery disease,
arthritis, ea diseases or		dyslipidemia, gallstones, osteoarthritis, degenerative
diseases or		22
		diseases or disorders. Preferred indications include
neopiasms		neoplasms and cancer, such as, lymphoma, leukemia and

					breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
0 0	H5AVA08	768	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al	A preterred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Tmmune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and reating ioint damage in patients with rheumatorial arthritis
				Gene 66:1-10 (1998); Cullen and Malm, Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells	An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia,

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				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
			•		hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below
					under "Infectious Disease").
378	HSAVA08	892	Production of IL-5	IL-5 FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins secreted by	includes a method for inhibiting (e.g., reducing) IL-5
				TH2 cells, mast cells, basophils, and	production. An alternative highly preferred embodiment of
				eosinophils that stimulate eosinophil	the invention includes a method for stimulating (e.g.,
				function and B cell Ig production and	increasing) IL-5 production. A highly preferred
				promote polarization of CD4+ cells into	embodiment of the invention includes a method for
				TH2 cells are well known in the art and	stimulating (e.g., increasing) immunoglobulin production.
				may be used or routinely modified to	An alternative highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for inhibiting (e.g.,
				invention (including antibodies and	ou
				agonists or antagonists of the invention) to	preferred indication includes allergy. A highly
				mediate immunomodulation, stimulate	preferred indication includes asthma. A highly
				immune cell function, modulate B cell Ig	preferred indication includes rhinitis. An additional
				production, modulate immune cell	highly preferred indication is infection (e.g., an infectious
				polarization, and/or mediate humoral or	disease as described below under "Infectious Disease"),
				cell-mediated immunity. Exemplary	and inflammation and inflammatory disorders.
				assays that test for immunomodulatory	Preferred indications include blood disorders (e.g., as
				proteins evaluate the production of	described below under "Immune Activity", "Blood-
				cytokines, such as IL-5, and the	Related Disorders", and/or "Cardiovascular Disorders").
				stimulation of eosinophil function and B	Preferred indications include autoimmune diseases (e.g.,
				cell Ig production. Such assays that may	rheumatoid arthritis, systemic lupus erythematosis,
				be used or routinely modified to test	multiple sclerosis and/or as described below) and
				immunomodulatory activity of	immunodeficiencies (e.g., as described below).
				polypeptides of the invention (including	Preferred indications include neoplastic diseases (e.g.,
				antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and/or as described
				the invention) include the assays disclosed	below under "Hyperproliterative Disorders"). Preferred

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				in Miraglia et al., J Biomolecular	indications include neoplasms and cancers, such as,
				Screening 4:193-204 (1999); Rowland et	leukemia, lymphoma, melanoma, and prostate, breast,
				al., "Lymphocytes: a practical approach"	lung, colon, pancreatic, esophageal, stomach, brain, liver
				Chapter 6:138-160 (2000); Ohshima et al.,	and urinary cancer. Other preferred indications include
				Blood 92(9):3338-3345 (1998); Jung et al.,	benign dysproliferative disorders and pre-neoplastic
			-	Eur J Immunol 25(8):2413-2416 (1995);	conditions, such as, for example, hyperplasia, metaplasia,
				Mori et al., J Allergy Clin Immunol 106(1	and/or dysplasia. Preferred indications include anemia,
				Pt 2):558-564 (2000); and Koning et al.,	pancytopenia, leukopenia, thrombocytopenia, leukemias,
				Cytokine 9(6):427-436 (1997), the	Hodgkin's disease, acute lymphocytic anemia (ALL),
				contents of each of which are herein	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				incorporated by reference in its entirety.	arthritis, AIDS, granulomatous disease, inflammatory
				Human T cells that may be used according	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
-				to these assays may be isolated using	immune reactions to transplanted organs and tissues,
				techniques disclosed herein or otherwise	hemophilia, hypercoagulation, diabetes mellitus,
				known in the art. Human T cells are	endocarditis, meningitis, and Lyme Disease.
-				primary human lymphocytes that mature in	
				the thymus and express a T cell receptor	
				and CD3, CD4, or CD8. These cells	
				mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory factors.	
379	HSAVW42	893	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
			Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
				example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
				measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
				have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
				calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
				extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
		· · · · · · · · · · · · · · · · · · ·		can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,
				activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
				pathways and alterations in cell functions.	stroke, and other diseases and disorders as described in the
				Exemplary assays that may be used or	"Cardiovascular Disorders" section below), dyslipidemia,

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endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.
routinely modified to measure calcium flux by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Satin LS, et al., Endocrinology, 136(10):4589-601 (1995);Mogami H, et al., Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al., Cell Calcium 1989 Nov-Dec;10(8):535-41 (1989), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin, or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely
	Production of ICAM-1
	894
	HSAWN53
	380

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).
	Production of ICAM-1
	\$68
	HSAWZ40
	381

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A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious biseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications associated with insulin resistance.	
Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used	according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain
Stimulation of insulin secretion from pancreatic beta cells.	
968	
HSAYC41	
382	

				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	
383	HSDZM54	897	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
			•	antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,
				used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,
				killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel disease, neutropenia,

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					neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
384	HSHBF76	868	Endothelial Cell Apoptosis	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary endothelial cells that may be used according to these assays	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. An alternative highly preferred below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular
				include bovine aortic endothelial cells (bAEC), which are an example of	disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic

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		endothelial cells which line blood vessels	overload, and/or as described below under
		and are involved in functions that include.	"Cardiovascular Disorders"). Highly preferred indications
		but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic
		vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such
		immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels
			themselves, such as of the arteries, capillaries, veins and/or
			lymphatics). Highly preferred are indications that
			stimulate angiogenesis and/or cardiovascularization.
			Highly preferred are indications that inhibit angiogenesis
			and/or cardiovascularization. Highly preferred
			indications include antiangiogenic activity to treat solid
			tumors, leukemias, and Kaposi's sarcoma, and retinal
			disorders. Highly preferred indications include neoplasms
			and cancer, such as, Kaposi's sarcoma, hemangioma
			(capillary and cavernous), glomus tumors, telangiectasia,
			bacillary angiomatosis, hemangioendothelioma,
			angiosarcoma, haemangiopericytoma, lymphangioma,
			lymphangiosarcoma. Highly preferred indications also
			include cancers such as, prostate, breast, lung, colon,
			pancreatic, esophageal, stomach, brain, liver, and urinary
			cancer. Preferred indications include benign
			dysproliferative disorders and pre-neoplastic conditions,
			such as, for example, hyperplasia, metaplasia, and/or
			dysplasia. Highly preferred indications also include
			arterial disease, such as, atherosclerosis, hypertension,
			coronary artery disease, inflammatory vasculitides,
•			Reynaud's disease and Reynaud's phenomenom,
			aneurysms, restenosis; venous and lymphatic disorders
			such as thrombophlebitis, lymphangitis, and lymphedema;
			and other vascular disorders such as peripheral vascular
			disease, and cancer. Highly preferred indications also
			include trauma such as wounds, burns, and injured tissue
 •			(e.g., vascular injury such as, injury resulting from balloon
			angioplasty, and atheroschlerotic lesions), implant
	•		fixation, scarring, ischemia reperfusion injury, rheumatoid
			arthritis, cerebrovascular disease, renal diseases such as
			acute renal failure, and osteoporosis. Additional highly

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					preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory diseases, e.g., inflammatory bowel disease
384	HSHBF76	868	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders", and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below) and immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred indications include inflammation and inflammatory

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			immunomodulation and differentiation and	disorders. Additional highly preferred indications include
			modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
			Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
			immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
			production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
			the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
			proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
			Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
-			modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
			diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
		•	the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
			agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
			include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
			J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
			a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
-			(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
			158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
			each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
			reference in its entirety. Human dendritic	_
			cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
			assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
			disclosed herein or otherwise known in the	described below under "Infectious Disease").
			art. Human dendritic cells are antigen	
			presenting cells in suspension culture,	
			which, when activated by antigen and/or	
			cytokines, initiate and upregulate T cell	
-			proliferation and functional activities.	
385 HSIFG47	668	Endothelial Cell	Caspase Apoptosis. Assays for caspase	A highly preferred embodiment of the invention
		Apoptosis	apoptosis are well known in the art and	includes a method for stimulating endothelial cell growth.
			may be used or routinely modified to	An alternative highly preferred embodiment of the
-			assess the ability of polypeptides of the	invention includes a method for inhibiting endothelial cell
			invention (including antibodies and	growth. A highly preferred embodiment of the
			agonists or antagonists of the invention) to	invention includes a method for stimulating endothelial
			promote caspase protease-mediated	cell proliferation. An alternative highly preferred
			apoptosis. Induction of apoptosis in	metho
			endothelial cells supporting the vasculature	inhibiting endothelial cell proliteration. A highly

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	of tumors is associated with tumor	preferred embodiment of the invention includes a method
	regression due to loss of tumor blood	for stimulating apoptosis of endothelial cells. An
	supply. Exemplary assays for caspase	alternative highly preferred embodiment of the invention
	apoptosis that may be used or routinely	g (e.g
	modified to test capase apoptosis activity	apoptosis of endothelial cells. A highly preferred
	of polypeptides of the invention (including	embodiment of the invention includes a method for
	antibodies and agonists or antagonists of	stimulating angiogenisis. An alternative highly preferred
	the invention) include the assays disclosed	embodiment of the invention includes a method for
	in Lee et al., FEBS Lett 485(2-3): 122-126	inhibiting angiogenesis. A highly preferred
	(2000); Nor et al., J Vasc Res 37(3): 209-	embodiment of the invention includes a method for
	218 (2000); and Karsan and Harlan, J	reducing cardiac hypertrophy. An alternative highly
	Atheroscler Thromb 3(2): 75-80 (1996);	preferred embodiment of the invention includes a method
	the contents of each of which are herein	for inducing cardiac hypertrophy. Highly preferred
	incorporated by reference in its entirety.	indications include neoplastic diseases (e.g., as described
	Endothelial cells that may be used	below under "Hyperproliferative Disorders"), and
	according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,
	available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,
	sources). Exemplary endothelial cells that	cardiomyopathy, valvular regurgitation, left ventricular
	may be used according to these assays	dysfunction, atherosclerosis and atherosclerotic vascular
	include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac
	(bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic
	endothelial cells which line blood vessels	overload, and/or as described below under
	and are involved in functions that include,	"Cardiovascular Disorders"). Highly preferred indications
	but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic
	vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such
	immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels
		themselves, such as of the arteries, capillaries, veins and/or
		lymphatics). Highly preferred are indications that
		stimulate angiogenesis and/or cardiovascularization.
		Highly preferred are indications that inhibit angiogenesis
		and/or cardiovascularization. Highly preferred
		indications include antiangiogenic activity to treat solid
		tumors, leukemias, and Kaposi's sarcoma, and retinal
		disorders. Highly preferred indications include neoplasms
-		and cancer, such as, Kaposi's sarcoma, hemangioma
		(capillary and cavernous), glomus tumors, telangiectasia,
		bacillary angiomatosis, hemangioendothelioma,

					inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
386	HSJBY32	006	Endothelial Cell	Caspase Apoptosis. Assays for caspase	A highly preferred embodiment of the invention
			Apoptosis	apoptosis are well known in the art and	includes a method for stimulating endothelial cell growth.
				may be used or routinely modified to	An alternative highly preterred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for inhibiting endothelial cell
				invention (including antibodies and	growth. A highly preferred embodiment of the
				agonists or antagonists of the invention) to	invention includes a method for stimulating endothelial
				promote caspase protease-mediated	cell proliferation. An alternative highly preferred
				apoptosis. Induction of apoptosis in	embodiment of the invention includes a method for
				endothelial cells supporting the vasculature	inhibiting endothelial cell proliferation. A highly
				of tumors is associated with tumor	preferred embodiment of the invention includes a method
				regression due to loss of tumor blood	for stimulating apoptosis of endothelial cells. An
				supply. Exemplary assays for caspase	alternative highly preferred embodiment of the invention
				apoptosis that may be used or routinely	includes a method for inhibiting (e.g., decreasing)
				modified to test capase apoptosis activity	apoptosis of endothelial cells. A highly preferred
				of polypeptides of the invention (including	embodiment of the invention includes a method for
				antibodies and agonists or antagonists of	stimulating angiogenisis. An alternative highly preferred
				the invention) include the assays disclosed	embodiment of the invention includes a method for
				in Lee et al., FEBS Lett 485(2-3): 122-126	inhibiting angiogenesis. A highly preferred
				(2000); Nor et al., J Vasc Res 37(3): 209-	embodiment of the invention includes a method for
				218 (2000); and Karsan and Harlan, J	reducing cardiac hypertrophy. An alternative highly
				Atheroscler Thromb 3(2): 75-80 (1996);	preferred embodiment of the invention includes a method
				the contents of each of which are herein	for inducing cardiac hypertrophy. Highly preferred
				incorporated by reference in its entirety.	indications include neoplastic diseases (e.g., as described
				Endothelial cells that may be used	below under "Hyperproliferative Disorders"), and
				according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,
				available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,
				sources). Exemplary endothelial cells that	cardiomyopathy, valvular regurgitation, left ventricular
				may be used according to these assays	dysfunction, atherosclerosis and atherosclerotic vascular
				include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac
				(bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic
				endothelial cells which line blood vessels	overload, and/or as described below under
				and are involved in functions that include,	"Cardiovascular Disorders"). Highly preferred indications
				but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic
				vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such
				immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels

				themselves, such as of the arteries, capillaries, veins and/or
		-		Ivmnhatics). Highly preferred are indications that
	_			thingments): triging proteined and interesting that
				stimulate angiogenesis and/or cardiovascularization.
				Highly preferred are indications that inhibit angiogenesis
				and/or cardiovascularization. Highly preferred
				indications include antiangiogenic activity to treat solid
				tumors, leukemias, and Kaposi's sarcoma, and retinal
				disorders. Highly preferred indications include neoplasms
				and cancer, such as, Kaposi's sarcoma, hemangioma
				(capillary and cavernous), glomus tumors, telangiectasia,
				bacillary angiomatosis, hemangioendothelioma,
				angiosarcoma, haemangiopericytoma, lymphangioma,
				lymphangiosarcoma. Highly preferred indications also
				include cancers such as, prostate, breast, lung, colon,
				pancreatic, esophageal, stomach, brain, liver, and urinary
				cancer. Preferred indications include benign
			-	dysproliferative disorders and pre-neoplastic conditions,
				such as, for example, hyperplasia, metaplasia, and/or
				dysplasia. Highly preferred indications also include
				eas
				coronary artery disease, inflammatory vasculitides,
				Reynaud's disease and Reynaud's phenomenom,
				aneurysms, restenosis; venous and lymphatic disorders
				such as thrombophlebitis, lymphangitis, and lymphedema;
				and other vascular disorders such as peripheral vascular
				disease, and cancer. Highly preferred indications also
		·		include trauma such as wounds, burns, and injured tissue
				(e.g., vascular injury such as, injury resulting from balloon
				angioplasty, and atheroschlerotic lesions), implant
				fixation, scarring, ischemia reperfusion injury, rheumatoid
				arthritis, cerebrovascular disease, renal diseases such as
				acute renal failure, and osteoporosis. Additional highly
				graf
 				diabetic or other retinopathies, thrombotic and coagulative
				disorders, vascularitis, lymph angiogenesis, sexual
				disorders, age-related macular degeneration, and treatment
				/prevention of endometriosis and related conditions.

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according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,
available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,
sources). Exemplary endothelial cells that	cardiomyopathy, valvular regurgitation, left ventricular
may be used according to these assays	dysfunction, atherosclerosis and atherosclerotic vascular
include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac
 (bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic
endothelial cells which line blood vessels	overload, and/or as described below under
and are involved in functions that include,	"Cardiovascular Disorders"). Highly preferred indications
but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic
vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such
immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels
	themselves, such as of the arteries, capillaries, veins and/or
	lymphatics). Highly preferred are indications that
	stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms
	and cancer, such as, Kaposi's sarcoma, hemangioma
	(capillary and cavernous), glomus tumors, telangiectasia,
	bacillary angiomatosis, hemangioendothelioma,
	angiosarcoma, haemangiopericytoma, lymphangioma,
	lymphangiosarcoma. Highly preferred indications also
	include cancers such as, prostate, breast, lung, colon,
	pancreatic, esophageal, stomach, brain, liver, and urinary
	cancer. Preferred indications include benign
	dysproliferative disorders and pre-neoplastic conditions,
	such as, for example, hyperplasia, metaplasia, and/or
	dysplasia. Highly preferred indications also include
	arterial disease, such as, atherosclerosis, hypertension,
	coronary artery disease, inflammatory vasculitides,
	Reynaud's disease and Reynaud's phenomenom,
	aneurysms, restenosis; venous and lymphatic disorders
	such as thrombophlebitis, lymphangitis, and lymphedema;
	isor
	disease, and cancer. Highly preferred indications also

					include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammatory diseases, e.g., inflammatory bowel disease
387 HS	HSKDR27	901	Proliferation, differentiation, and/or cytokine production in immune cells (such as T-cells).	Kinase assays, for example kinase assays for members of the MAP kinase family (including p38, JAK, and ERK) are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, differentiation., and/or cytokine production in immune cells such as T-cells. Exemplary assays for MAP kinase family members that may be used or routinely modified to test polypeptides	and crown a charactery, and pain management. Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of inflammation, infection, allergy, asthma, autoimmunity, and cancer.

				of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Rincon M., Curr Opin Immunol; 13(3):339-345 (2001); Wang LH, et al., J Immunol, 162(7):3897-3904 (1999); Sakamoto H, et al., J Biol Chem, 275(46):35857-35862 (2000), the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells (for example, T-cells) that may be used according to these assays include the	
387 HSKDR27	727	106	Production of IL-4	IL-4 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immune cells, modulate immune cell polarization, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antaconists of the invention) include the	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-4 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-4 production. A highly preferred indication includes asthma. A highly preferred indication includes rhinits. Additional highly preferred indication include inflammation and inflammatory disorders. Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", preferred indications include blood-disorders"). Preferred indications include
				assays disclosed in Miraglia et al., J	autoimmune diseases (e.g., rheumatoid arthritis, systemic

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				Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194); Yssel et al., Res Immunol 144(8):610-616 (1993); Bagley et al., Nat Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
388	HSLHG78	902	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cell-

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				of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
				antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
				the invention) to mediate	indications include inflammation and inflammatory
				immunomodulation and differentiation and	disorders. Additional highly preferred indications include
				modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
				Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
				immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
				production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
				the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
				proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
				Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
				modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
				diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
				the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
				agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
				include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
				J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
				204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
				a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
				(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
				158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
				each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
				reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
				assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
				disclosed herein or otherwise known in the	described below under "Infectious Disease").
				art. Human dendritic cells are antigen	
				presenting cells in suspension culture,	
				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
388	HSLHG78	206	Production of MCP-1	MCP-1 FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins that are	includes a method for stimulating (e.g., increasing) MCP-1
				produced by a large variety of cells and act	production. An alternative highly preferred embodiment of
				to induce chemotaxis and activation of	the invention includes a method for inhibiting (e.g.,
				monocytes and T cells are well known in	reducing) MCP-1 production. A highly preferred
				the art and may be used or routinely	indication is infection (e.g., an infectious disease as

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				modified to assess the ability of	described below under "Infections Disease"). Additional
				nolymentides of the invention (including	highly preferred indications include inflammation and
				antihodies and agonists or antagonists of	inflammatory disorders Preferred indications include
				the invention) to mediate	Ť
				immunomodulation, induce chemotaxis,	Activity", "Blood-Related Disorders", and/or
				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
				Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
				production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
				Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
				Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
	•			al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,
				contents of each of which are herein	pancreatic, esophageal, stomach, brain, liver, and urinary
				incorporated by reference in its entirety.	cancer. Other preferred indications include benign
				Human dendritic cells that may be used	dysproliferative disorders and pre-neoplastic conditions,
				according to these assays may be isolated	such as, for example, hyperplasia, metaplasia, and/or
				using techniques disclosed herein or	dysplasia.
				otherwise known in the art. Human	
				dendritic cells are antigen presenting cells	
				in suspension culture, which, when	
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation	
				and functional activities.	
388	HSLHG78	905	Production of	MIP-1alpha FMAT. Assays for	A highly preferred embodiment of the invention
			MIP1alpha	immunomodulatory proteins produced by	includes a method for stimulating MIP1a production. An

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activated	activated dendritic cells that upregulate	alternative highly preferred embodiment of the invention
monocyte/	monocyte/macrophage and T cell	includes a method for inhibiting (e.g., reducing) MIP1a
chemotaxi	chemotaxis are well known in the art and	production. A highly preferred indication is infection
may be use	may be used or routinely modified to	(e.g., an infectious disease as described below under
assess the	assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
invention	invention (including antibodies and	blood disorders (e.g., as described below under "Immune
agonists or	agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
mediate in	mediate immunomodulation, modulate	"Cardiovascular Disorders"). Highly preferred indications
chemotaxi	chemotaxis, and modulate T cell	include autoimmune diseases (e.g., rheumatoid arthritis,
differentia	differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as
for immun	for immunomodulatory proteins evaluate	described below) and immunodeficiencies (e.g., as
the produc	the production of chemokines, such as	described below). Additional highly preferred indications
macrophag	macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
(MIP-1a),	(MP-1a), and the activation of	Preferred indications also include anemia, pancytopenia,
monocytes	monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute
assays that	assays that may be used or routinely	lymphocytic anemia (ALL), plasmacytomas, multiple
modified t	modified to test immunomodulatory and	myeloma, Burkitt's lymphoma, arthritis, AIDS,
chemotaxi	chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
invention	invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
agonists or	agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
include as	include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
J Biomole	J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
204(1999)	204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
a practical	a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
(2000); Sa	(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
Surg Ednb	Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
al., Transp	al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
Verhasselt	Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
2925 (199	2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
Biol 65:82	Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
each of wh	each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
reference	reference in its entirety. Human dendritic	dysplasia.
cells that r	cells that may be used according to these	
assays ma	assays may be isolated using techniques	
disclosed	disclosed herein or otherwise known in the	
art. Huma	art. Human dendritic cells are antigen	
presenting	presenting cells in suspension culture,	

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				which, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell proliferation and functional activities.	
389	HSLHX15	903	Upregulation of HLA-	HLA-DR FMAT. MHC class II is essential	Highly preferred indications include blood disorders
			DR and activation of T	for correct presentation of antigen to CD4+	(e.g., as described below under "Immune Activity",
			cells	T cells. Deregulation of MHC class II has	"Blood-Related Disorders", and/or "Cardiovascular
				been associated with autoimmune diseases	Disorders"). Highly preferred indications include
				(e.g., diabetes, rheumatoid arthritis,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				systemic lupus erythematosis, and multiple	lupus erythematosis, multiple sclerosis and/or as described
				sclerosis). Assays for immunomodulatory	below) and immunodeficiencies (e.g., as described below),
				proteins expressed on MHC class II	boosting a T cell-mediated immune response, and
				expressing T cells and antigen presenting	alternatively, suppressing a T cell-mediated immune
				cells are well known in the art and may be	response. A highly preferred indication is diabetes
				used or routinely modified to assess the	mellitus. An additional highly preferred indication
				ability of polypeptides of the invention	is a complication associated with diabetes (e.g., diabetic
				(including antibodies and agonists or	retinopathy, diabetic nephropathy, kidney disease (e.g.,
				antagonists of the invention) to modulate	renal failure, nephropathy and/or other diseases and
				the activation of T cells, and/or mediate	disorders as described in the "Renal Disorders" section
				humoral or cell-mediated immunity.	below), diabetic neuropathy, nerve disease and nerve
				Exemplary assays that test for	damage (e.g., due to diabetic neuropathy), blood vessel
				immunomodulatory proteins evaluate the	blockage, heart disease, stroke, impotence (e.g., due to
				upregulation of MHC class II products,	diabetic neuropathy or blood vessel blockage), seizures,
				such as HLA-DR antigens, and the	mental confusion, drowsiness, nonketotic hyperglycemic-
				activation of T cells. Such assays that may	hyperosmolar coma, cardiovascular disease (e.g., heart
				be used or routinely modified to test	disease, atherosclerosis, microvascular disease,
				immunomodulatory activity of	hypertension, stroke, and other diseases and disorders as
				polypeptides of the invention (including	described in the "Cardiovascular Disorders" section
				antibodies and agonists or antagonists of	below), dyslipidemia, endocrine disorders (as described in
				the invention) include, for example, the	the "Endocrine Disorders" section below), neuropathy,
				assays disclosed in Miraglia et al., J	vision impairment (e.g., diabetic retinopathy and
				Biomolecular Screening 4:193-204 (1999);	blindness), ulcers and impaired wound healing, and
				Rowland et al., "Lymphocytes: a practical	infection (e.g., infectious diseases and disorders as
				approach" Chapter 6:138-160 (2000);	described in the "Infectious Diseases" section below,
				Lamour et al., Clin Exp Immunol	especially of the urinary tract and skin), carpal tunnel
				89(2):217-222 (1992); Hurme and Sihvola,	syndrome and Dupuytren's contracture). An
				Immunol Lett 20(3):217-222 (1989);	additional highly preferred indication is obesity and/or
				Ganspacher and Zier, Cell Immunol	complications associated with obesity. Additional highly

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			Histochem Cytochem 40(11):1675-1683, the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. An additional preferred indication is infection (e.g., AIDS, and/or as described below under "Infectious Disease"). Preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"), and neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancer, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkiti's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammatory disorders, and asthma and allergy.
390 HSNAP85	904	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis,

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systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplastic diseases (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, and allergy. An additional preferred indication is infectiou (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. Highly preferred indications include blood disorders (e.g., as described below under "Immune
growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	CD154 FMAT. CD154 (a.k.a., CD40L) expression is induced following activation of T cells. Interraction between CD154 and CD40 on B cells is required for correct antibody class switching and germinal center formation. Mutations in CD154 are
	Upregulation of CD154 and activation of T cells
	905
	HSNAZ09
	391

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	linked to immunodeficiencies and	Activity", "Blood-Kelated Disorders", and/or
	increased susceptibility to infections.	"Cardiovascular Disorders"), and intection (e.g., as
	Assays for immunomodulatory proteins	described below under "Infectious Disease"). Highly
	important for antibody class switching and	nd preferred indications include autoimmune diseases (e.g.,
	TH1 function and expressed on activated T	1 T rheumatoid arthritis, systemic lupus erythematosis,
	helper lymphocytes are well known in the	
	art and may be used or routinely modified	
	to assess the ability of polypeptides of the	
	invention (including antibodies and	
****	agonists or antagonists of the invention) to	
	modulate the activation of T cells,	
	modulate antibody class switching,	below under "Hyperproliferative Disorders"). Highly
	mediate TH1 function, and/or mediate	preferred indications include neoplasms, such as, for
	humoral or cell-mediated immunity.	example, leukemia, lymphoma, and prostate, breast, lung,
	Exemplary assays that test for	colon, pancreatic, esophageal, stomach, brain, liver and
	immunomodulatory proteins evaluate the	
	upregulation of cell surface markers, such	ch dysproliferative disorders and pre-neoplastic conditions,
	as CD154, and the activation of T cells.	
	Such assays that may be used or routinely	
	modified to test immunomodulatory	pancytopenia, leukopenia, thrombocytopenia, leukemias,
	activity of polypeptides of the invention	
	(including antibodies and agonists or	
	antagonists of the invention) include, for	
	example, the assays disclosed in Miraglia	
	et al., J Biomolecular Screening 4:193-204	
	(1999); Rowland et al., "Lymphocytes: a	
	practical approach" Chapter 6:138-160	endocarditis, meningitis, Lyme Disease, inflammation and
	(2000); Mackey et al., J Leukoc Biol	inflammatory disorders, and asthma and allergy.
	63(4):418:428 (1998); and Skov et al.,	
	164(7):3500-3505 (2000), the contents of)f
	each of which are herein incorporated by	
_	reference in its entirety. Human T cells	
	that may be used according to these assays	Sví
	may be isolated using techniques disclosed	pa
	herein or otherwise known in the art.	
	Human T cells are primary human	-
	lymphocytes that mature in the thymus and	pu-

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				express a T Cell receptor and CD3, CD4,	
				or CD8. These cells mediate humoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
392	HSNBM34	906	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription via	through the DMEF1 response element are	An additional highly preferred indication is a complication
			DMEF1 response	well-known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			element in adipocytes	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
			and pre-adipocytes	polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to activate the DMEF1	neuropathy, nerve disease and nerve damage (e.g., due to
				response element in a reporter construct	diabetic neuropathy), blood vessel blockage, heart disease,
				such as that containing the GLUT4	stroke, impotence (e.g., due to diabetic neuropathy or
				promoter) and to regulate insulin	blood vessel blockage), seizures, mental confusion,
				production. The DMEF1 response	drowsiness, nonketotic hyperglycemic-hyperosmolar
				element is present in the GLUT4 promoter	coma, cardiovascular disease (e.g., heart disease,
				and binds to MEF2 transcription factor and	atherosclerosis, microvascular disease, hypertension,
	•			another transcription factor that is required	stroke, and other diseases and disorders as described in the
				for insulin regulation of Glut4 expression	"Cardiovascular Disorders" section below), dyslipidemia,
				in skeletal muscle. GLUT4 is the primary	endocrine disorders (as described in the "Endocrine
				insulin-responsive glucose transporter in	Disorders" section below), neuropathy, vision impairment
				fat and muscle tissue. Exemplary assays	(e.g., diabetic retinopathy and blindness), ulcers and
				that may be used or routinely modified to	impaired wound healing, and infection (e.g., infectious
				test for DMEF1 response element activity	diseases and disorders as described in the "Infectious
				(in adipocytes and pre-adipocytes) by	Diseases" section below, especially of the urinary tract and
				polypeptides of the invention (including	tunne
				antibodies and agonists or antagonists of	contracture). An additional highly preferred
				the invention) include assays disclosed	indication is obesity and/or complications associated with
				inThai, M.V., et al., J Biol Chem,	obesity. Additional highly preferred indications include
				273(23):14285-92 (1998); Mora, S., et al.,	weight loss or alternatively, weight gain. Aditional
				J Biol Chem, 275(21):16323-8 (2000); Liu,	highly preferred indications are complications associated
				M.L., et al., J Biol Chem, 269(45):28514-	with insulin resistance.
				21 (1994); "Identification of a 30-base pair	
				regulatory element and novel DNA	
				binding protein that regulates the human	
				GLUT4 promoter in transgenic mice", J	

				Biol Chem. 2000 Aug 4;275(31):23666-	
				73; Berger, et al., Gene 66:1-10 (1988);	
				and, Cullen, B., et al., Methods in	
				Enzymol. 216:362-368 (1992), the	
				contents of each of which is herein	
				incorporated by reference in its entirety.	
				Adipocytes and pre-adipocytes that may be	
				used according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
•				may be routinely generated. Exemplary	
				cells that may be used according to these	
•				assays include the mouse 3T3-L1 cell line	
				which is an adherent mouse preadipocyte	
				cell line. Mouse 3T3-L1 cells are a	
				continuous substrain of 3T3 fibroblasts	
		,		developed through clonal isolation. These	
				cells undergo a pre-adipocyte to adipose-	
				like conversion under appropriate	
				differentiation culture conditions.	
393	HSOAH16	206	Production of	IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
		-	cells	considered to be a proinflammatory	An alternative highly preferred embodiment of the
				cytokine. IFNg promotes TH1 and	invention includes a method for inhibiting the production
				inhibits TH2 differentiation; promotes	of IFNg. Highly preferred indications include blood
				IgG2a and inhibits IgE secretion; induces	disorders (e.g., as described below under "Immune
				macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
				MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
				immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
				T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
				of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
				helper cell functions are well known in the	Highly preferred indications include autoimmune disease
				art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
				invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
				agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
				mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
				inflammatory activities, modulate TH2	indications include inflammation and inflammatory

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			helper cell function, and/or mediate	disorders. Additional preferred indications include
			humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
			Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
			immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
		***	production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
			gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
			cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
			routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
			immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
			polypeptides of the invention (including	include benign dysproliferative disorders and pre-
			antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
			the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
			in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
			Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
			Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
			J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
			Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
			(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
			15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
			(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
			of each of which are herein incorporated	
			by reference in its entirety. Human T cells	
			that may be used according to these assays	
			may be isolated using techniques disclosed	
			herein or otherwise known in the art.	
			Human T cells are primary human	
			lymphocytes that mature in the thymus and	
			express a T Cell receptor and CD3, CD4,	
			or CD8. These cells mediate humoral or	
			cell-mediated immunity and may be	
			preactivated to enhance responsiveness to	
			immunomodulatory factors.	
394 HSQBF66	806	Production of IL-5	IL-5 FMAT. Assays for	A highly preferred embodiment of the invention
			immunomodulatory proteins secreted by	includes a method for inhibiting (e.g., reducing) IL-5
			TH2 cells, mast cells, basophils, and	production. An alternative highly preferred embodiment of
			eosinophils that stimulate eosinophil	the invention includes a method for stimulating (e.g.,

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function and B call In production and	increasing) II - 5 production A highly preferred
promote polarization of CD4+ cells into	Ĕ
TH2 cells are well known in the art and	stimulating (e.g., increasing) immunoglobulin production.
may be used or routinely modified to	An alternative highly preferred embodiment of the
assess the ability of polypeptides of the	9
invention (including antibodies and	decreasing) immunoglobulin production. A highly
agonists or antagonists of the invention) to	
mediate immunomodulation, stimulate	
immune cell function, modulate B cell Ig	preferred indication includes rhinitis. An additional
production, modulate immune cell	highly preferred indication is infection (e.g., an infectious
polarization, and/or mediate humoral or	disease as described below under "Infectious Disease"),
cell-mediated immunity. Exemplary	and inflammation and inflammatory disorders.
assays that test for immunomodulatory	Preferred indications include blood disorders (e.g., as
proteins evaluate the production of	described below under "Immune Activity", "Blood-
cytokines, such as IL-5, and the	Related Disorders", and/or "Cardiovascular Disorders").
stimulation of eosinophil function and B	Preferred indications include autoimmune diseases (e.g.,
cell Ig production. Such assays that may	rheumatoid arthritis, systemic lupus erythematosis,
be used or routinely modified to test	multiple sclerosis and/or as described below) and
immunomodulatory activity of	immunodeficiencies (e.g., as described below).
polypeptides of the invention (including	Preferred indications include neoplastic diseases (e.g.,
antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and/or as described
the invention) include the assays disclosed	below under "Hyperproliferative Disorders"). Preferred
in Miraglia et al., J Biomolecular	indications include neoplasms and cancers, such as,
Screening 4:193-204 (1999); Rowland et	leukemia, lymphoma, melanoma, and prostate, breast,
al., "Lymphocytes: a practical approach"	lung, colon, pancreatic, esophageal, stomach, brain, liver
Chapter 6:138-160 (2000); Ohshima et al.,	and urinary cancer. Other preferred indications include
Blood 92(9):3338-3345 (1998); Jung et al.,	benign dysproliferative disorders and pre-neoplastic
Eur J Immunol 25(8):2413-2416 (1995);	conditions, such as, for example, hyperplasia, metaplasia,
Mori et al., J Allergy Clin Immunol 106(1	and/or dysplasia. Preferred indications include anemia,
Pt 2):558-564 (2000); and Koning et al.,	pancytopenia, leukopenia, thrombocytopenia, leukemias,
Cytokine 9(6):427-436 (1997), the	Hodgkin's disease, acute lymphocytic anemia (ALL),
contents of each of which are herein	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
incorporated by reference in its entirety.	arthritis, AIDS, granulomatous disease, inflammatory
Human T cells that may be used according	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
to these assays may be isolated using	immune reactions to transplanted organs and tissues,
techniques disclosed herein or otherwise	hemophilia, hypercoagulation, diabetes mellitus,
known in the art. Human I cells are	endocarditis, meningitis, and Lyme Disease.

				primary human lymphocytes that mature in the thymus and express a T cell receptor	
				and CD3, CD4, or CD8. These cells	
				mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
200	30000011	000	3	immunomodulatory factors.	A himbly manformed ambadiment of the invention
393	HSQDO85	906	Activation of	Kinase assay. JINK and p38 kinase assays	A nigniy presented embodiment of the invention
			Endothelial Cell p38 or	for signal transduction that regulate cell	includes a method for stimulating endothelial cell growth.
			JNK Signaling	proliferation, activation, or apoptosis are	An alternative highly preferred embodiment of the
			Pathway.	well known in the art and may be used or	
				routinely modified to assess the ability of	growth. A highly preferred embodiment of the
				polypeptides of the invention (including	invention includes a method for stimulating endothelial
				antibodies and agonists or antagonists of	cell proliferation. An alternative highly preferred
				the invention) to promote or inhibit cell	embodiment of the invention includes a method for
				proliferation, activation, and apoptosis.	inhibiting endothelial cell proliferation. A highly
				Exemplary assays for JNK and p38 kinase	preferred embodiment of the invention includes a method
				activity that may be used or routinely	for stimulating apoptosis of endothelial cells. An
				modified to test JNK and p38 kinase-	alternative highly preferred embodiment of the invention
				induced activity of polypeptides of the	includes a method for inhibiting (e.g., decreasing)
				invention (including antibodies and	apoptosis of endothelial cells. A highly preferred
				agonists or antagonists of the invention)	embodiment of the invention includes a method for
				include the assays disclosed in Forrer et	stimulating (e.g., increasing) endothelial cell activation.
				al., Biol Chem 379(8-9):1101-1110	An alternative highly preferred embodiment of the
				(1998); Gupta et al., Exp Cell Res 247(2):	invention includes a method for inhibiting (e.g.,
				495-504 (1999); Kyriakis JM, Biochem	ctivatio
				Soc Symp 64:29-48 (1999); Chang and	endothelial cells. A highly preferred embodiment of
				Karin, Nature 410(6824):37-40 (2001);	the invention includes a method for stimulating
				and Cobb MH, Prog Biophys Mol Biol	angiogenisis. An alternative highly preferred embodiment
				71(3-4):479-500 (1999); the contents of	of the invention includes a method for inhibiting
	,			each of which are herein incorporated by	angiogenesis. A highly preferred embodiment of the
				reference in its entirety. Endothelial cells	invention includes a method for reducing cardiac
				that may be used according to these assays	hypertrophy. An alternative highly preferred embodiment
	-			are publicly available (e.g., through the	of the invention includes a method for inducing cardiac
				ATCC). Exemplary endothelial cells that	hypertrophy. Highly preferred indications include
				may be used according to these assays	neoplastic diseases (e.g., as described below under
				include human umbilical vein endothelial	"Hyperproliferative Disorders"), and disorders of the

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cells (HUVEC), which are endothelial	cardiovascular system (e.g., heart disease, congestive heart
cells which line venous blood vessels, and	failure, hypertension, aortic stenosis, cardiomyopathy,
are involved in functions that include, but	valvular regurgitation, left ventricular dysfunction,
are not limited to, angiogenesis, vascular	atherosclerosis and atherosclerotic vascular disease,
permeability, vascular tone, and immune	diabetic nephropathy, intracardiac shunt, cardiac
cell extravasation.	hypertrophy, myocardial infarction, chronic hemodynamic
	overload, and/or as described below under
	"Cardiovascular Disorders"). Highly preferred indications
	include cardiovascular, endothelial and/or angiogenic
	disorders (e.g., systemic disorders that affect vessels such
	as diabetes mellitus, as well as diseases of the vessels
	themselves, such as of the arteries, capillaries, veins and/or
	lymphatics). Highly preferred are indications that
	stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms
	and cancer, such as, Kaposi's sarcoma, hemangioma
	(capillary and cavernous), glomus tumors, telangiectasia,
	bacillary angiomatosis, hemangioendothelioma,
	angiosarcoma, haemangiopericytoma, lymphangioma,
	lymphangiosarcoma. Highly preferred indications also
	include cancers such as, prostate, breast, lung, colon,
	pancreatic, esophageal, stomach, brain, liver, and urinary
	cancer. Preferred indications include benign
	dysproliferative disorders and pre-neoplastic conditions,
	such as, for example, hyperplasia, metaplasia, and/or
	dysplasia. Highly preferred indications also include
	arterial disease, such as, atherosclerosis, hypertension,
	coronary artery disease, inflammatory vasculitides,
	Reynaud's disease and Reynaud's phenomenom,
	aneurysms, restenosis; venous and lymphatic disorders
	such as thrombophlebitis, lymphangitis, and lymphedema;
	and other vascular disorders such as peripheral vascular
	disease, and cancer. Highly preferred indications also

					include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below). Additional preferred indications include inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease, and pain management.
396	HSQES57	910	Production of TNF alpha by dendritic cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and

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				assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
				proteins evaluate the production of	Additional highly preferred indications include
				cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
				alpha (TNFa), and the induction or	joint damage in patients with rheumatoid arthritis. An
	·			inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
				response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
				routinely modified to test	leukemia, lymphoma, and/or as described below under
				immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
				polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
•				antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
				the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
				Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
				4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
				"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
				Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
				al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
				(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
				(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
				herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
				entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
				be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
				isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
				or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
				dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
•				in suspension culture, which, when	Disease").
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation	
				and functional activities.	
396 HS(HSQES57	910	Activation of Natural	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			Killer Cell ERK	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating natural killer cell
			Signaling Pathway.	transduction that regulate cell proliferation	proliferation. An alternative highly preferred embodiment
				or differentiation are well known in the art	ಡ
				and may be used or routinely modified to	killer cell proliferation. A highly preferred
				assess the ability of polypeptides of the	embodiment of the invention includes a method for

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				invention (including antibodies and	stimulating natural killer cell differentiation. An
				agonists or antagonists of the invention) to	alternative highly preferred embodiment of the invention
				promote or inhibit cell proliferation,	includes a method for inhibiting natural killer cell
				activation, and differentiation. Exemplary	differentiation. Highly preferred indications include
				assays for ERK kinase activity that may be	neoplastic diseases (e.g., as described below under
				used or routinely modified to test ERK	"Hyperproliferative Disorders"), blood disorders (e.g., as
				kinase-induced activity of polypeptides of	described below under "Immune Activity",
				the invention (including antibodies and	"Cardiovascular Disorders", and/or "Blood-Related
				agonists or antagonists of the invention)	Disorders"), immune disorders (e.g., as described below
	-			include the assays disclosed in Forrer et	., as
	_			al., Biol Chem 379(8-9):1101-1110	described below under "Infectious Disease"). Preferred
	_			(1998); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., as described
	_			64:29-48 (1999); Chang and Karin, Nature	below under "Immune Activity", "Blood-Related
				410(6824):37-40 (2001); and Cobb MH,	Disorders", and/or "Cardiovascular Disorders"). Highly
	_			Prog Biophys Mol Biol 71(3-4):479-500	preferred indications include autoimmune diseases (e.g.,
	_			(1999); the contents of each of which are	rheumatoid arthritis, systemic lupus erythematosis,
				herein incorporated by reference in its	multiple sclerosis and/or as described below) and
_				entirety. Natural killer cells that may be	immunodeficiencies (e.g., as described below). Additional
				used according to these assays are publicly	highly preferred indications include inflammation and
				available (e.g., through the ATCC).	inflammatory disorders. Highly preferred indications
				Exemplary natural killer cells that may be	also include cancers such as, kidney, melanoma, prostate,
				used according to these assays include the	breast, lung, colon, pancreatic, esophageal, stomach,
				human natural killer cell lines (for	brain, liver, urinary cancer, lymphoma and leukemias.
				example, NK-YT cells which have	Other preferred indications include benign dysproliferative
				cytolytic and cytotoxic activity) or primary	disorders and pre-neoplastic conditions, such as, for
				NK cells.	example, hyperplasia, metaplasia, and/or dysplasia.
					Other highly preferred indications include, pancytopenia,
					leukopenia, leukemias, Hodgkin's disease, acute
					lymphocytic anemia (ALL), arthritis, asthma, AIDS,
					granulomatous disease, inflammatory bowel disease,
					sepsis, psoriasis, immune reactions to transplanted organs
					and tissues, endocarditis, meningitis, Lyme Disease, and
					allergies.
397 HS	HSRBE06	911	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
				(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			In immune cells (such	be used of routinely modified to assess the	IIIVEIIUUII IIICIUUCS a IIICIIIOU IOI SUIIIUIauiig (C.B.,

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		as T-cells)	ability of nolymentides of the invention	increasing) TNF alpha production Preferred indications
			(including antibodies and agonists or	include blood disorders (e.g., as described below under
			antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
			the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
			the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
			growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
			transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
			used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
			activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
			invention (including antibodies and	immune response. Additional highly preferred indications
			agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
			include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
			Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
			Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
			Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
			85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
			Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
			content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
			incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
			cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
			assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
			the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
			may be used according to these assays	pre-neoplastic conditions, such as, for example,
			include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
			2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
			with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				anemia (ALL), plasmacytomas, multiple myeloma,
				Burkitt's lymphoma, arthritis, AIDS, granulomatous
				disease, inflammatory bowel disease, neutropenia,
				neutrophilia, psoriasis, suppression of immune reactions to
				transplanted organs and tissues, hemophilia,
				hypercoagulation, diabetes mellitus, endocarditis,
				meningitis, Lyme Disease, cardiac reperfusion injury, and
				asthma and allergy. An additional preferred indication
				is infection (e.g., an infectious disease as described below
				under "Infectious Disease").
398 HSSDI26	912	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention

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	and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
	participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
	and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
	role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
	cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
	of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
	disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
	chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
	Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
	differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
	a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
	expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
-	cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
	are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
	or routinely modified to assess the ability	preferred indications also include boosting a B cell-
	of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
	antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
	the invention) to mediate	indications include inflammation and inflammatory
	immunomodulation and differentiation and	disorders. Additional highly preferred indications include
	modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
	Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
	immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
	production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
	the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
	proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
	Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
	modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
	diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
	the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
	agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
	include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
	J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
	204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
	a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
	(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
	158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
	each of which are herein incorporated by	transplanted organs and tissues, hemophilia,

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			reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
398 HSSDI26	912	Activation of Endothelial Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) endothelial cell activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) the activation of and/or inactivating endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a method for stimulating angiogenesis.
			reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that	invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include

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	may be used according to these assays	neoplastic diseases (e.g., as described below under
	include human umbilical vein endothelial	"Hyperproliferative Disorders"), and disorders of the
	cells (HUVEC), which are endothelial	cardiovascular system (e.g., heart disease, congestive heart
	cells which line venous blood vessels, and	failure, hypertension, aortic stenosis, cardiomyopathy,
	are involved in functions that include, but	valvular regurgitation, left ventricular dysfunction,
	are not limited to, angiogenesis, vascular	atherosclerosis and atherosclerotic vascular disease,
	permeability, vascular tone, and immune	diabetic nephropathy, intracardiac shunt, cardiac
	cell extravasation.	hypertrophy, myocardial infarction, chronic hemodynamic
		overload, and/or as described below under
		"Cardiovascular Disorders"). Highly preferred indications
		include cardiovascular, endothelial and/or angiogenic
		disorders (e.g., systemic disorders that affect vessels such
		as diabetes mellitus, as well as diseases of the vessels
		themselves, such as of the arteries, capillaries, veins and/or
		lymphatics). Highly preferred are indications that
		stimulate angiogenesis and/or cardiovascularization.
		Highly preferred are indications that inhibit angiogenesis
		and/or cardiovascularization. Highly preferred
		indications include antiangiogenic activity to treat solid
		tumors, leukemias, and Kaposi's sarcoma, and retinal
		disorders. Highly preferred indications include neoplasms
		and cancer, such as, Kaposi's sarcoma, hemangioma
		(capillary and cavernous), glomus tumors, telangiectasia,
		bacillary angiomatosis, hemangioendothelioma,
		angiosarcoma, haemangiopericytoma, lymphangioma,
		lymphangiosarcoma. Highly preferred indications also
		include cancers such as, prostate, breast, lung, colon,
		pancreatic, esophageal, stomach, brain, liver, and urinary
		cancer. Preferred indications include benign
		dysproliferative disorders and pre-neoplastic conditions,
		such as, for example, hyperplasia, metaplasia, and/or
		dysplasia. Highly preferred indications also include
		arterial disease, such as, atherosclerosis, hypertension,
		coronary artery disease, inflammatory vasculitides,
		Reynaud's disease and Reynaud's phenomenom,
		aneurysms, restenosis; venous and lymphatic disorders
		such as thrombophlebitis, lymphangitis, and lymphedema;

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(e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication	is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of inflammation, infection, allergy, asthma, autoimmunity, and cancer.
used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	Kinase assays, for example kinase assays for members of the MAP kinase family (including p38, JAK, and ERK) are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell
	Proliferation, differentiation, and/or cytokine production in immune cells (such as T-cells).
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				proliferation, differentiation., and/or cytokine production in immune cells such as T-cells. Exemplary assays for MAP kinase family members that may be used or routinely modified to test polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Rincon M., Curr Opin Immunol; 13(3):339-345 (2001); Wang LH, et al., J Immunol, 162(7):3897-3904 (1999); Sakamoto H, et al., J Biol Chem, 275(46):35857-35862 (2000), the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells (for example, T-cells) that may be used according to these assays include the	
400	HSSEF77	914	Insulin Secretion	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious

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diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple
Shimizu, H., et al., Endocr J, 47(3):261-9 (2000); Salapatek, A.M., et al., Mol Endocrinol, 13(8):1305-17 (1999); Filipsson, K., et al., Ann NY Acad Sci, 865:441-4 (1998); Olson, L.K., et al., J Biol Chem, 271(28):16544-52 (1996); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for
	Activation of transcription through serum response element in immune cells (such as T-cells).
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				transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication asthma and allergy.
401	HSSFE38	915	Upregulation of CD152 and activation of T cells	CD152 FMAT. CD152 (a.k.a. CTLA-4) expression is restricted to activated T cells. CD152 is a negative regulator of T cell proliferation. Reduced CD152 expression has been linked to hyperproliferative and autoimmune diseases. Overexpression of CD152 may lead to impaired	In mection (e.g., an infectious disease as described below under "Infectious Disease"). A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a invention includes a method for inhibiting T cell proliferation. An alternative highly preferred embodiment

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 imminorodalatory proteins important in		or the invention includes a include for standard a con-
	_	profile audit. Ingility preferred indications include
 the maintenance of T cell homeostasis and		blood disorders (e.g., as described below under "Immune
expressed almost exclusively on CD4+ and		Activity", "Blood-Related Disorders", and/or
CD8+ T cells are well known in the art and		"Cardiovascular Disorders"), Highly preferred indications
may be used or routinely modified to		include autoimmune diseases (e.g., rheumatoid arthritis,
assess the ability of polypeptides of the		systemic lupus erythematosis, multiple sclerosis and/or as
invention (including antibodies and		described below), immunodeficiencies (e.g., as described
agonists or antagonists of the invention) to		below), boosting a T cell-mediated immune response, and
modulate the activation of T cells,	_	suppressing a T cell-mediated immune response.
maintain T cell homeostasis, and/or		Highly preferred indications include neoplastic diseases
mediate humoral or cell-mediated		(e.g., leukemia, lymphoma, and/or as described below
immunity. Exemplary assays that test for		under "Hyperproliferative Disorders"). Additionally,
 immunomodulatory proteins evaluate the		highly preferred indications include neoplasms and
upregulation of cell surface markers, such		cancers, such as, for example, leukemia, lymphoma,
as CD152, and the activation of T cells.		melanoma, and prostate, breast, lung, colon, pancreatic,
 Such assays that may be used or routinely	<u>~</u>	esophageal, stomach, brain, liver and urinary cancer.
modified to test immunomodulatory		Other preferred indications include benign dysproliferative
activity of polypeptides of the invention		disorders and pre-neoplastic conditions, such as, for
(including antibodies and agonists or		example, hyperplasia, metaplasia, and/or dysplasia.
 antagonists of the invention) include, for		Preferred indications include anemia, pancytopenia,
example, the assays disclosed in Miraglia		leukopenia, thrombocytopenia, Hodgkin's disease, acute
 et al., J Biomolecular Screening 4:193-204		lymphocytic anemia (ALL), plasmacytomas, multiple
(1999); Rowland et al., "Lymphocytes: a		myeloma, Burkitt's lymphoma, arthritis, AIDS,
 practical approach" Chapter 6:138-160		granulomatous disease, inflammatory bowel disease,
(2000); McCoy et al., Immunol Cell Biol		sepsis, neutropenia, neutrophilia, psoriasis, immune
 77(1):1-10 (1999); Oostervegal et al., Curr		reactions to transplanted organs and tissues, hemophilia,
 Opin Immunol 11(3):294-300 (1999); and	덛	hypercoagulation, diabetes mellitus, endocarditis,
 Saito T, Curr Opin Immunol 10(3):313-		meningitis, Lyme Disease, inflammation and
321 (1998), the contents of each of which		inflammatory disorders, and asthma and allergy. An
are herein incorporated by reference in its		additional preferred indication is infection (e.g., as
entirety. Human T cells that may be used		described below under "Infectious Disease").
according to these assays may be isolated	be isolated	
using techniques disclosed herein or	in or	
otherwise known in the art. Human T cells	man T cells	
are primary human lymphocytes that	s that	
mature in the thymus and express a 1 Cell	ss a T Cell	

				receptor and CD3, CD4, or CD8. These	
				cells mediate humoral or cell-mediated	
				immunity and may be preactivated to	
				enhance responsiveness to	
				immunomodulatory tactors.	
405	HSSG158	916	Production of ICAM-1	Assays for measuring expression of	Preferred embodiments of the invention include using
				ICAM-1 are well-known in the art and	polypeptides of the invention (or antibodies, agonists, or
				may be used or routinely modified to	antagonists thereof) in detection, diagnosis, prevention,
				assess the ability of polypeptides of the	and/or treatment of Inflammation, Vascular Disease,
				invention (including antibodies and	Athereosclerosis, Restenosis, and Stroke
				agonists or antagonists of the invention) to	
				regulate ICAM-1 expression. Exemplary	
				assays that may be used or routinely	
				modified to measure ICAM-1 expression	
				include assays disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281 (2001); and,	
				Miyamoto K. et al., Am J Pathol.	
				156(5) 1733-1739 (2000), the contents of	
				10(2):11:1:1:1:1:1:1:1:1:1:1:1:1:1:1:1:1:1:	
				each of which is herein incorporated by	
				reference in its entirety. Cells that may be	
				used according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				cells that may be used according to these	
				assavs include microvascular endothelial	
				cells (MVEC).	
403	HSWBE76	917	Production of IL-5	IL-5 FMAT. Assays for	A highly preferred embodiment of the invention
				immunomodulatory proteins secreted by	includes a method for inhibiting (e.g., reducing) IL-5
				TH2 cells, mast cells, basophils, and	production. An alternative highly preferred embodiment of
				eosinophils that stimulate eosinophil	the invention includes a method for stimulating (e.g.,
				function and B cell Ig production and	increasing) IL-5 production. A highly preferred
				promote polarization of CD4+ cells into	embodiment of the invention includes a method for
				TH2 cells are well known in the art and	stimulating (e.g., increasing) immunoglobulin production.
				may be used or routinely modified to	An alternative highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for inhibiting (e.g.,
				invention (including antibodies and	decreasing) immunoglobulin production. A highly
				agonists or antagonists of the invention) to	preferred indication includes allergy. A highly

mediate immunomodulation, stimulate	
immune cell function, modulate B cell Ig	preferred indication includes rhinitis. An additional
production, modulate immune cell	highly preferred indication is infection (e.g., an infectious
polarization, and/or mediate humoral or	disease as described below under "Infectious Disease"),
cell-mediated immunity. Exemplary	and inflammation and inflammatory disorders.
assays that test for immunomodulatory	Preferred indications include blood disorders (e.g., as
proteins evaluate the production of	described below under "Immune Activity", "Blood-
cytokines, such as IL-5, and the	Related Disorders", and/or "Cardiovascular Disorders").
stimulation of eosinophil function and B	Preferred indications include autoimmune diseases (e.g.,
 cell Ig production. Such assays that may	rheumatoid arthritis, systemic lupus erythematosis,
be used or routinely modified to test	multiple sclerosis and/or as described below) and
immunomodulatory activity of	immunodeficiencies (e.g., as described below).
polypeptides of the invention (including	Preferred indications include neoplastic diseases (e.g.,
antibodies and agonists or antagonists of	leukemia, lymphoma, melanoma, and/or as described
the invention) include the assays disclosed	below under "Hyperproliferative Disorders"). Preferred
in Miraglia et al., J Biomolecular	indications include neoplasms and cancers, such as,
Screening 4:193-204 (1999); Rowland et	leukemia, lymphoma, melanoma, and prostate, breast,
al., "Lymphocytes: a practical approach"	lung, colon, pancreatic, esophageal, stomach, brain, liver
Chapter 6:138-160 (2000); Ohshima et al.,	and urinary cancer. Other preferred indications include
Blood 92(9):3338-3345 (1998); Jung et al.,	benign dysproliferative disorders and pre-neoplastic
Eur J Immunol 25(8):2413-2416 (1995);	conditions, such as, for example, hyperplasia, metaplasia,
Mori et al., J Allergy Clin Immunol 106(1	and/or dysplasia. Preferred indications include anemia,
Pt 2):558-564 (2000); and Koning et al.,	pancytopenia, leukopenia, thrombocytopenia, leukemias,
 Cytokine 9(6):427-436 (1997), the	Hodgkin's disease, acute lymphocytic anemia (ALL),
 contents of each of which are herein	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
 incorporated by reference in its entirety.	arthritis, AIDS, granulomatous disease, inflammatory
Human T cells that may be used according	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
to these assays may be isolated using	immune reactions to transplanted organs and tissues,
techniques disclosed herein or otherwise	hemophilia, hypercoagulation, diabetes mellitus,
known in the art. Human T cells are	endocarditis, meningitis, and Lyme Disease.
primary human lymphocytes that mature in	
the thymus and express a T cell receptor	
and CD3, CD4, or CD8. These cells	
mediate humoral or cell-mediated	
immunity and may be preactivated to	
enhance responsiveness to	
immunomodulatory factors.	

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404	HSXCP38	918	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
				modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
-				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,
			-	used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,
				killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous
				activity.	disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
		-			hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and

asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method
	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include Aortic Smooth Muscle Cells (AOSMC); such as bovine AOSMC.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase
	Production of ICAM-1	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
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	405	406

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activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) endothelial cell activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) the activation of and/or inactivating endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating angiogenesis. An alternative highly preferred embodiment of the invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins andor hymbarics). Highly preferred are indications than sumbarics). Highly preferred are indications than sumbarics).
	stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred

tumors, leukemias, and Kaposi's sarcoma, and retinal disorders. Highly preferred indications include neoplasms	and cancer, such as, Kaposi's sarcoma, hemangioma	(capillary and cavernous), glomus tumors, telangiectasia,	bacillary angiomatosis, hemangioendothelioma,	angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver, and urinary	cancer. Preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions,	such as, for example, hyperplasia, metaplasia, and/or	dysplasia. Highly preferred indications also include	arterial disease, such as, atherosclerosis, hypertension,	coronary artery disease, inflammatory vasculitides,	Reynaud's disease and Reynaud's phenomenom,	aneurysms, restenosis; venous and lymphatic disorders	such as thrombophlebitis, lymphangitis, and lymphedema;	and other vascular disorders such as peripheral vascular	disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue	(e.g., vascular injury such as, injury resulting from balloon	angioplasty, and atheroschlerotic lesions), implant	fixation, scarring, ischemia reperfusion injury, rheumatoid	arthritis, cerebrovascular disease, renal diseases such as	acute renal failure, and osteoporosis. Additional highly	preferred indications include stroke, graft rejection,	diabetic or other retinopathies, thrombotic and coagulative	disorders, vascularitis, lymph angiogenesis, sexual	disorders, age-related macular degeneration, and treatment	/prevention of endometriosis and related conditions.	Additional highly preferred indications include fibromas,	heart disease, cardiac arrest, heart valve disease, and	vascular disease. Preferred indications include blood	disorders (e.g., as described below under "Immune	Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"). Preferred indications include
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autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease, and pain management.	Production of IL.4 FMAT. Assays for includes a method for simulating (e.g., increasing) IL.4 macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells and promote polarization of CD4+ cells into TH2 cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to sesses the ability of polypeptides of the invention (including mithodies ashman and may be used or routinely modified to test immunomodulation, stimulate immune cell polarization cells. modulate immune cell polarization cells. modulate immune cell polarization cells. modulate immune cell polarization of colls. modulate immune cell polarization of cells. modulate immune cell polarization of cells. modulate immune cell collegists and mast cells. Such assay that test for immunomodulation group proteins evaluate the stimulation of immune cells. such as B cells. T cells, macrophages and mast cells. Such assay that may be used or routinely modified to test immunomodulation production of cytokines, such as IL.4, and urinary cancer. Other preferred indications include bening dysproliferative disorders. Preferred indications include sassays dated for continely and urinary cancer. Other preferred indications include bening dysproliferative disorders. Preferred indications include to activity of polypeptides of the invention (including anniodicated or routinely modified to test immunomodulatory proteins evaluate the stimulation of immune cells, such as B bening dysproliferative disorders. Preferred indications include the assays data cells and urinary cancer. Other preferred indications include bening dysproliferative disorders. Preferred indications include the assays data cells and urinary cancer. Other preferred indications include the assays data cells and urinary cancer. Other preferred indications include the assays data cells and urinary cancer. Other preferred indications include automatical approach. Chapter 6:138-18-100 (2000); Rowland at all and may test of routinely
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granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-5 production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-5 production. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) immunoglobulin production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) immunoglobulin production. A highly preferred indication includes altergy. A highly preferred indication includes asthma. A highly preferred indication includes rhinitis. An additional highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and
Immunol 1(3):257-261 (2000); and van der Graaff et al., Rheumatology (Oxford) 38(3):214-220 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	IL-5 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells, mast cells, basophils, and eosinophils that stimulate eosinophil function and B cell Ig production and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cell function, modulate B cell Ig production, modulate immune cell polarization, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-5, and the stimulation of eosinophil function and B cell Ig production. Such assays that may be used or routinely modified to test
	Production of IL-5
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immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar
immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Ohshima et al., Blood 92(9):3338-3345 (1998); Jung et al., Eur J Immunol 25(8):2413-2416 (1995); Mori et al., J Allergy Clin Immunol 106(1 Pt 2):558-564 (2000); and Koning et al., Cytokine 9(6):427-436 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated to	immunomodulatory factors. Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain
	Stimulation of insulin secretion from pancreatic beta cells.
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				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
				2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
				Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
				Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
				(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
				Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
				(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
	**			available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
409	HT5FX79	923	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
				or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
				and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
				assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
				invention (including antibodies and	differentiation. An alternative highly preferred

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agonists or antagonists of the invention) to	es a
promote or innibit cell proliteration, activation, and differentiation. Exemplary	innibiting adipocyte differentiation. A nigniy preferred embodiment of the invention includes a method
assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine

					Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and
					impaired wound healing, infection (e.g., infectious diseases and disorders as described in the "Infectious
					Diseases" section below (particularly of the urinary tract and skin) An additional highly preferred indication is
					ю/р
					Additional highly preferred indications include weight loss
					or alternatively, weight gain. Additional highly
					ons are
					insulin resistance. Additional highly preferred
					indications are disorders of the musculoskeletal systems
					hies
					described herein. Additional highly preferred
					indications include, hypertension, coronary artery disease,
					dyslipidemia, gallstones, osteoarthritis, degenerative
					arthritis, eating disorders, fibrosis, cachexia, and kidney
					diseases or disorders. Preferred indications include
					neoplasms and cancer, such as, lymphoma, leukemia and
					breast, colon, and kidney cancer. Additional preferred
					indications include melanoma, prostate, lung, pancreatic,
					esophageal, stomach, brain, liver, and urinary cancer.
					Highly preferred indications include lipomas and
					liposarcomas. Other preferred indications include benign
					dysproliferative disorders and pre-neoplastic conditions,
					such as, for example, hyperplasia, metaplasia, and/or
+					dysplasia.
410	HT5GR59	924	Activation of	Assays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
			transcription through	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
			AP1 response element	known in the art and may be used or	blood disorders (e.g., as described below under "Immune
			in immune cells (such	routinely modified to assess the ability of	Activity", "Cardiovascular Disorders", and/or "Blood-
			as T-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious
				antibodies and agonists or antagonists of	disease as described below under "Infectious Disease").
				the invention) to modulate growth and	Highly preferred indications include autoimmune diseases
				other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				transcription through the AP1 response	multiple sclerosis and/or as described below) and
				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional

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				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
				assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
				Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory
				assays are publicly available (e.g., through	bowel disease, sepsis, psoriasis, suppression of immune
				the ATCC). Exemplary mouse T cells that	reactions to transplanted organs and tissues, endocarditis,
				may be used according to these assays	meningitis, and Lyme Disease.
				include the CTLL cell line, which is an IL-	
				2 dependent suspension-culture cell line	
				with cytotoxic activity.	
410	HT5GR59	924	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
			pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
				of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
				secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
				is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
				insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
				pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
				glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
				proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
				key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
				assays that may be used or routinely	stroke, and other diseases and disorders as described in the
				modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,

				secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
				polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
				2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
				Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
				Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
				(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
				Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
				(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
-				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
411	HTAEI78	925	Upregulation of HLA-	HLA-DR FMAT. MHC class II is essential	Highly preferred indications include blood disorders
			DR and activation of T	for correct presentation of antigen to CD4+	(e.g., as described below under "Immune Activity",
			cells	T cells. Deregulation of MHC class II has	"Blood-Related Disorders", and/or "Cardiovascular
				been associated with autoimmune diseases	Disorders"). Highly preferred indications include
				(e.g., diabetes, rheumatoid arthritis,	autoimmune diseases (e.g., rheumatoid arthritis, systemic
				systemic lupus erythematosis, and multiple	lupus erythematosis, multiple sclerosis and/or as described
				sclerosis). Assays for immunomodulatory	below) and immunodeficiencies (e.g., as described below),
				proteins expressed on MHC class II	boosting a T cell-mediated immune response, and
				expressing T cells and antigen presenting	alternatively, suppressing a T cell-mediated immune
				cells are well known in the art and may be	response. A highly preferred indication is diabetes
			3.33	used or routinely modified to assess the	mellitus. An additional highly preferred indication

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	is a complication associated with diadetes (e.g., diadetic
(including antibodies and agonists or	retinopathy, diabetic nephropathy, kidney disease (e.g.,
antagonists of the invention) to modulate	renal failure, nephropathy and/or other diseases and
the activation of T cells, and/or mediate	disorders as described in the "Renal Disorders" section
humoral or cell-mediated immunity.	below), diabetic neuropathy, nerve disease and nerve
 Exemplary assays that test for	damage (e.g., due to diabetic neuropathy), blood vessel
 immunomodulatory.proteins evaluate the	blockage, heart disease, stroke, impotence (e.g., due to
 upregulation of MHC class II products,	diabetic neuropathy or blood vessel blockage), seizures,
 such as HLA-DR antigens, and the	mental confusion, drowsiness, nonketotic hyperglycemic-
activation of T cells. Such assays that may	hyperosmolar coma, cardiovascular disease (e.g., heart
be used or routinely modified to test	disease, atherosclerosis, microvascular disease,
immunomodulatory activity of	hypertension, stroke, and other diseases and disorders as
polypeptides of the invention (including	described in the "Cardiovascular Disorders" section
antibodies and agonists or antagonists of	below), dyslipidemia, endocrine disorders (as described in
the invention) include, for example, the	the "Endocrine Disorders" section below), neuropathy,
assays disclosed in Miraglia et al., J	vision impairment (e.g., diabetic retinopathy and
Biomolecular Screening 4:193-204 (1999);	blindness), ulcers and impaired wound healing, and
Rowland et al., "Lymphocytes: a practical	infection (e.g., infectious diseases and disorders as
approach" Chapter 6:138-160 (2000);	described in the "Infectious Diseases" section below,
Lamour et al., Clin Exp Immunol	especially of the urinary tract and skin), carpal tunnel
89(2):217-222 (1992); Hurme and Sihvola,	syndrome and Dupuytren's contracture). An
Immunol Lett 20(3):217-222 (1989);	additional highly preferred indication is obesity and/or
Gansbacher and Zier, Cell Immunol	complications associated with obesity. Additional highly
117(1):22-34 (1988); and Itoh et al., J	preferred indications include weight loss or alternatively,
Histochem Cytochem 40(11):1675-1683,	weight gain. Aditional highly preferred indications
the contents of each of which are herein	are complications associated with insulin resistance.
 incorporated by reference in its entirety.	Additional highly preferred indications are disorders of the
 Human T cells that may be used according	musculoskeletal systems including myopathies, muscular
to these assays may be isolated using	dystrophy, and/or as described herein.
techniques disclosed herein or otherwise	additional preferred indication is infection (e.g., AIDS,
known in the art. Human T cells are	and/or as described below under "Infectious Disease").
primary human lymphocytes that mature in	Preferred indications include endocrine disorders (e.g., as
the thymus and express a T Cell receptor	described below under "Endocrine Disorders"), and
and CD3, CD4, or CD8. These cells	neoplastic diseases (e.g., leukemia, lymphoma, and/or as
mediate humoral or cell-mediated	described below under "Hyperproliferative Disorders").
immunity and may be preactivated to	Preferred indications include neoplasms and cancer, such
enhance responsiveness to	as, for example, leukemia, lymphoma, and prostate, breast,

				immunomodulatory factors.	lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, endocarditis, meningitis, Lyme Disease, inflammation and allergy.
412 H	HTDAA78	926	Production of ICAM-1	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Rolfe BE, et al., Atherosclerosis, 149(1):99-110 (2000); Panettieri RA Jr, et al., J Immunol, 154(5):2358-2365 (1995); and, Grunstein MM, et al., Am J Physiol Lung Cell Mol Physiol, 278(6):L1154-L1163 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include shortic Smooth Muscle Cells (AOSMC):	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Vascular Disease, Atherosclerosis, Restenosis, Stroke, and Asthma.

			3	such as bovine AOSMC.	
412	HTDAA78	926	Activation of Natural	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			Killer Cell ERK	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating natural killer cell
		-	Signaling Pathway.	transduction that regulate cell proliferation	proliferation. An alternative highly preferred embodiment
				or differentiation are well known in the art	of the invention includes a method for inhibiting natural
				and may be used or routinely modified to	killer cell proliferation. A highly preferred
				assess the ability of polypeptides of the	embodiment of the invention includes a method for
				invention (including antibodies and	stimulating natural killer cell differentiation. An
				agonists or antagonists of the invention) to	alternative highly preferred embodiment of the invention
				promote or inhibit cell proliferation,	includes a method for inhibiting natural killer cell
				activation, and differentiation. Exemplary	differentiation. Highly preferred indications include
			··· <u></u>	assays for ERK kinase activity that may be	neoplastic diseases (e.g., as described below under
				used or routinely modified to test ERK	"Hyperproliferative Disorders"), blood disorders (e.g., as
				kinase-induced activity of polypeptides of	described below under "Immune Activity",
				the invention (including antibodies and	"Cardiovascular Disorders", and/or "Blood-Related
				agonists or antagonists of the invention)	Disorders"), immune disorders (e.g., as described below
				include the assays disclosed in Forrer et	under "Immune Activity") and infections (e.g., as
				al., Biol Chem 379(8-9):1101-1110	described below under "Infectious Disease"). Preferred
				(1998); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., as described
				64:29-48 (1999); Chang and Karin, Nature	below under "Immune Activity", "Blood-Related
				410(6824):37-40 (2001); and Cobb MH,	Disorders", and/or "Cardiovascular Disorders"). Highly
				Prog Biophys Mol Biol 71(3-4):479-500	preferred indications include autoimmune diseases (e.g.,
				(1999); the contents of each of which are	rheumatoid arthritis, systemic lupus erythematosis,
				herein incorporated by reference in its	multiple sclerosis and/or as described below) and
				entirety. Natural killer cells that may be	immunodeficiencies (e.g., as described below). Additional
				used according to these assays are publicly	highly preferred indications include inflammation and
				available (e.g., through the ATCC).	inflammatory disorders. Highly preferred indications
				Exemplary natural killer cells that may be	also include cancers such as, kidney, melanoma, prostate,
				used according to these assays include the	breast, lung, colon, pancreatic, esophageal, stomach,
				human natural killer cell lines (for	brain, liver, urinary cancer, lymphoma and leukemias.
				example, NK-YT cells which have	Other preferred indications include benign dysproliferative
				cytolytic and cytotoxic activity) or primary	disorders and pre-neoplastic conditions, such as, for
				NK cells.	example, hyperplasia, metaplasia, and/or dysplasia.
		-			Other highly preferred indications include, pancytopenia,
					leukopenia, leukemias, Hodgkin's disease, acute
					lymphocytic anemia (ALL), arthritis, asthma, AIDS,
					granulomatous disease, inflammatory bowel disease,

					sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and allergies.
413	HTEAG62	927	Activation of Adipocyte PI3 Kinase Signalling	Kinase assay. Kinase assays, for example an GSK-3 assays, for PI3 kinase signal	A highly preferred embodiment of the invention includes a method for increasing adipocyte survival An
			Fathway	transduction that regulate glucose metabolism and cell survival are well-	atternative ingniy preferred embodiment of the invention includes a method for decreasing adipocyte survival. A
				known in the art and may be used or	preferred embodiment of the invention includes a method
				routinely modified to assess the ability of	for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a
				antibodies and agonists or antagonists of	method for inhibiting adipocyte proliferation. A
				the invention) to promote or inhibit	preferred embodiment of the invention includes a method
				glucose metabolism and cell survival.	for stimulating adipocyte differentiation. An alternative
				Exemplary assays for P13 kinase activity)Clu
		·····		that hidy be used of fourniery modified to	incurou for minibiling authoryte differentiation. Aligniy arreferred indications include andomine disorders (e.g., oc.
				polypeptides of the invention (including	described below under "Endocrine Disorders").
				antibodies and agonists or antagonists of	Preferred indications include neoplastic diseases (e.g.,
				the invention) include assays disclosed in	lipomas, liposarcomas, and/or as described below under
				Forrer et al., Biol Chem 379(8-9):1101-	"Hyperproliferative Disorders"), blood disorders (e.g.,
				1110 (1998); Nikoulina et al., Diabetes	hypertension, congestive heart failure, blood vessel
				49(2):263-271 (2000); and Schreyer et al.,	blockage, heart disease, stroke, impotence and/or as
				Diabetes 48(8):1662-1666 (1999), the	described below under "Immune Activity",
				contents of each of which are herein	"Cardiovascular Disorders", and/or "Blood-Related
				incorporated by reference in its entirety.	Disorders"), immune disorders (e.g., as described below
				Mouse adipocyte cells that may be used	under "Immune Activity"), neural disorders (e.g., as
				according to these assays are publicly	described below under "Neural Activity and Neurological
				available (e.g., through the ATCC).	on (e.g
				Exemplary mouse adipocyte cells that may	<u>`</u>
				be used according to these assays include	is diabetes mellitus. An additional highly preferred
				3T3-L1 cells. 3T3-L1 is an adherent	indication is a complication associated with diabetes (e.g.,
				mouse preadipocyte cell line that is a	diabetic retinopathy, diabetic nephropathy, kidney disease
				continous substrain of 3T3 fibroblast cells	(e.g., renal failure, nephropathy and/or other diseases and
				developed through clonal isolation and	disorders as described in the "Renal Disorders" section
			-	undergo a pre-adipocyte to adipose-like	below), diabetic neuropathy, nerve disease and nerve
				conversion under appropriate	damage (e.g, due to diabetic neuropathy), blood vessel
				differentiation conditions known in the art.	blockage, heart disease, stroke, impotence (e.g., due to

			diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hyperension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection blindness), ulcers and disorders as described in the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity and/or complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Highly preferred indications include melanoma, lymphoma, leukemia and breast, colon, and kidney diseases or disorders. Highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and preneoplastic conditions, such as, for example, hyperplasia,
413 HTEAG62 927	7 Regulation of transcription of Malic	Assays for the regulation of transcription of Malic Enzyme are well-known in the art	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication

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Dagumo in polinocates	to be used or routinely modified to	associated with diabetes (e.g. diabetic retinopathy
 Langline in adipocytes	and may be used of todament incomments of the	diabetic nentronathy kidney disease (e.g. renal failure
	assess the annual or polypopulates of the	napolic inchinopanty, without diseases and disorders as
	anonists or antagonists of the invention) to	described in the "Renal Disorders" section below), diahetic
	regulate transcription of Malic Enzyme, a	neuronathy, nerve disease and nerve damage (e.g., due to
	key enzyme in linogenesis. Malic enzyme	diabetic neuropathy), blood vessel blockage, heart disease,
	is involved in lipogenesisand its expression	stroke, impotence (e.g., due to diabetic neuropathy or
	is stimulted by insulin. ME promoter	blood vessel blockage), seizures, mental confusion,
	contains two direct repeat (DR1)- like	drowsiness, nonketotic hyperglycemic-hyperosmolar
	elements MEp and MEd identified as	coma, cardiovascular disease (e.g., heart disease,
	putative PPAR response elements. ME	atherosclerosis, microvascular disease, hypertension,
	promoter may also responds to AP1 and	stroke, and other diseases and disorders as described in the
	other transcription factors. Exemplary	"Cardiovascular Disorders" section below), dyslipidemia,
	assays that may be used or routinely	endocrine disorders (as described in the "Endocrine
	modified to test for regulation of	Disorders" section below), neuropathy, vision impairment
	transcription of Malic Enzyme (in	(e.g., diabetic retinopathy and blindness), ulcers and
	adipoocytes) by polypeptides of the	impaired wound healing, and infection (e.g., infectious
	invention (including antibodies and	diseases and disorders as described in the "Infectious
	agonists or antagonists of the invention)	Diseases" section below, especially of the urinary tract and
	include assays disclosed in: Streeper, R.S.,	skin), carpal tunnel syndrome and Dupuytren's
	et al., Mol Endocrinol, 12(11):1778-91	contracture). An additional highly preferred
	(1998); Garcia-Jimenez, C., et al., Mol	indication is obesity and/or complications associated with
	Endocrinol, 8(10):1361-9 (1994); Barroso,	obesity. Additional highly preferred indications include
	1., et al., J Biol Chem, 274(25):17997-8004	weight loss or alternatively, weight gain. Aditional
	(1999); Ijpenberg, A., et al., J Biol Chem,	highly preferred indications are complications associated
	272(32):20108-20117 (1997); Berger, et	with insulin resistance.
	al., Gene 66:1-10 (1988); and, Cullen, B.,	
	et al., Methods in Enzymol. 216:362–368	
	(1992), the contents of each of which is	
	herein incorporated by reference in its	
	entirety. Hepatocytes that may be used	
	according to these assays are publicly	
	available (e.g., through the ATCC) and/or	
	may be routinely generated. Exemplary	
	hepatocytes that may be used according to	
	these assays includes the H4IIE rat liver	
	hepatoma cell line.	

Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Neurological Diseases and Disorders (e.g. Alzheimer's Disease, Parkinson's Disease, Brain Cancer, Seizures).
Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of neuronal genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gill JS, et al.,
Production of ICAM-1	Activation of transcription through NFKB response element in neuronal cells (such as SKNMC cells).
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				Naurabial Dia 7(4):448 461 (2000).	
				Neurobiol Dis, /(4).446-401 (2000),	
				Lamatam M, et al., J Diol Chem,	
				7/4(13):8531-8538 (1999); Berger et al.,	
				Gene 66:1-10 (1998); Cullen and Malm,	
				Methods in Enzymol 216:362-368 (1992);	
				Henthorn et al., Proc Natl Acad Sci USA	
				85:6342-6346 (1988); Valle Blazquez et	
				al, Immunology 90(3):455-460 (1997);	
			-	Aramburau et al., J Exp Med 82(3):801-	
				810 (1995); and Fraser et al., 29(3):838-	
				844 (1999), the contents of each of which	
				are herein incorporated by reference in its	
				entirety. Neuronal cells that may be used	
				according to these assays are publicly	
				available (e.g., through the ATCC).	
				Exemplary neuronal cells that may be used	
				according to these assays include the	
				SKNMC neuronal cell line.	
416	HTEDF18	930	Production of	MIP-1alpha FMAT. Assays for	A highly preferred embodiment of the invention
			MIP1alpha	immunomodulatory proteins produced by	includes a method for stimulating MIP1a production. An
				activated dendritic cells that upregulate	alternative highly preferred embodiment of the invention
				monocyte/macrophage and T cell	includes a method for inhibiting (e.g., reducing) MIP1a
				chemotaxis are well known in the art and	production. A highly preferred indication is infection
				may be used or routinely modified to	(e.g., an infectious disease as described below under
				assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
				invention (including antibodies and	blood disorders (e.g., as described below under "Immune
				agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
				mediate immunomodulation, modulate	"Cardiovascular Disorders"). Highly preferred indications
				chemotaxis, and modulate T cell	include autoimmune diseases (e.g., rheumatoid arthritis,
·				differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as
				for immunomodulatory proteins evaluate	described below) and immunodeficiencies (e.g., as
				the production of chemokines, such as	described below). Additional highly preferred indications
				macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
				(MIP-1a), and the activation of	Preferred indications also include anemia, pancytopenia,
				monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute
		-		assays that may be used or routinely	lymphocytic anemia (ALL), plasmacytomas, multiple
		-1		modified to test immunomodulatory and	myeloma, Burkitt's lymphoma, arthritis, AIDS,

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				chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
417	HTEDJ28	931	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for stimulating the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly

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agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
publicly available (e.g., through the	described below under "Infectious Disease").
ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
that may be used according to these assays	additional highly preferred indication is a complication
include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,
	endocrine disorders (as described in the "Endocrine
	Disorders" section below), neuropathy, vision impairment
	(e.g., diabetic retinopathy and blindness), ulcers and
	impaired wound healing, infection (e.g., infectious
	diseases and disorders as described in the "Infectious
	Diseases" section below (particularly of the urinary tract
	and skin). An additional highly preferred indication is
	obesity and/or complications associated with obesity.

					Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dyspralasia
417	HTEDJ28	931	Activation of transcription through NFAT response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention)	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infectiou Diseases (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include neoplastic diseases (e.g., Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example,

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			include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
HTEDS12	932	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention, or promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders").

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	(1998): Le Marchand-Britstel Y. Exn Clin	diseases (e.g. linomas, linosarcomas, and/or as described
	Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
	(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
	64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
	410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
	Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
-	(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
	herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
	entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
	be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
	publicly available (e.g., through the	described below under "Infectious Disease").
	ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus.
	that may be used according to these assays	additional highly preferred indication is a complication
	include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
	adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
	cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		"Cardiovascular Disorders" section below), dyslipidemia,
		endocrine disorders (as described in the "Endocrine
		Disorders" section below), neuropathy, vision impairment
		(e.g., diabetic retinopathy and blindness), ulcers and
		impaired wound healing, infection (e.g., infectious
		diseases and disorders as described in the "Infectious
		sect
		and skin). An additional highly preferred indication is
		obesity and/or complications associated with obesity.
		ndicat
		or alternatively, weight gain. Additional highly
		preferred indications are complications associated with

				insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Preferred indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or
419 HTEED26	933	Activation of transcription through GAS response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Fnzymol 216-362-368 (1992).	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include hood disorders.

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				Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.	"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
420	HTEED26	934	Activation of transcription through GAS response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or

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				85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary mouse T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the CTLL cell line, which is a suspension culture of IL-2 dependent cytotoxic T cells.	"Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
421	HTEEF26	935	Production of MIP lalpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention)	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MIP1a production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammatory disorders. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues.

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			include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
			204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
			a practical approach" Chapter 6:138-160	્હં
			(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
			Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
			al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
			Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
		*****	2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
			Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
	-		each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
			reference in its entirety. Human dendritic	dysplasia.
			cells that may be used according to these	
			assays may be isolated using techniques	
			disclosed herein or otherwise known in the	
			art. Human dendritic cells are antigen	
			presenting cells in suspension culture,	
			which, when activated by antigen and/or	
	-		cytokines, initiate and upregulate T cell	
			proliferation and functional activities.	
422 HTEEF26	936	Production of	MIP-1alpha FMAT. Assays for	A highly preferred embodiment of the invention
		MIPlalpha	immunomodulatory proteins produced by	includes a method for stimulating MIP1a production. An
			activated dendritic cells that upregulate	alternative highly preferred embodiment of the invention
			monocyte/macrophage and T cell	includes a method for inhibiting (e.g., reducing) MIP1a
-			chemotaxis are well known in the art and	production. A highly preferred indication is infection
			may be used or routinely modified to	(e.g., an infectious disease as described below under
			assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
			invention (including antibodies and	blood disorders (e.g., as described below under "Immune
	•		agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
			mediate immunomodulation, modulate	"Cardiovascular Disorders"). Highly preferred indications
			chemotaxis, and modulate T cell	include autoimmune diseases (e.g., rheumatoid arthritis,
			differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as
			for immunomodulatory proteins evaluate	described below) and immunodeficiencies (e.g., as
			the production of chemokines, such as	described below). Additional highly preferred indications
			macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
			(MIP-1a), and the activation of	Preferred indications also include anemia, pancytopenia,
			monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute

				assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-	immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and
				204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described
				(2000); Satthaporn and Eremin, J R Coll Sure Ednb 45(1):9-19 (2001): Drakes et	below under "Hyperproliferative Disorders"). Highly preferred indications include neonlasms and cancers such
				al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
				Verhasselt et al., J Immunol 158:2919- 2925 (1997): and Nardelli et al. 11 eukoc	pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benion
				Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
				each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
				reference in its entirety. Human dendritic	dysplasia.
				cells that may be used according to these	
				disclosed herein or otherwise leaves in the	
				disclosed liefelli of other wise known in the	
				art. numan uchunine cens are anugen	
				presenting cells in suspension culture,	
				wnich, when activated by antigen and/or	
				cytokines, initiate and upregulate T cell	
Ť	200	100		proliferation and functional activities.	
423 HIEE	HIEEW69	93/	Activation of	Assays for the activation of transcription	Preferred indications include blood disorders (e.g., as
			transcription through	through the cAMP response element are	described below under "Immune Activity", "Blood-
			cAMP response	well-known in the art and may be used or	Related Disorders", and/or "Cardiovascular Disorders"),
			element in immune	routinely modified to assess the ability of	and infection (e.g., an infectious disease as described
			cells (such as T-cells).	polypeptides of the invention (including	below under "Infectious Disease"). Preferred
				antibodies and agonists or antagonists of	indications include autoimmune diseases (e.g., rheumatoid
				the invention) to increase cAMP, bind to	arthritis, systemic lupus erythematosis, multiple sclerosis
				CREB transcription factor, and modulate	and/or as described below), immunodeficiencies (e.g., as
				expression of genes involved in a wide	described below), boosting a T cell-mediated immune
				variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune
				assays for transcription through the cAMP	response. Additional preferred indications include
				response element that may be used or	inflammation and inflammatory disorders. Highly

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				routinely modified to test cAMP-response	preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Highly preferred
				agonists or antagonists of the invention)	indications include neoplasms and cancers, such as,
				include assays disclosed in Berger et al.,	leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's
				Gene 66:1-10 (1998); Cullen and Malm,	lymphoma, non-Hodgkins lymphoma, Hodgkin's disease),
				Methods in Enzymol 216:362-368 (1992);	melanoma, and prostate, breast, lung, colon, pancreatic,
				Henthorn et al., Proc Natl Acad Sci USA	esophageal, stomach, brain, liver and urinary cancer.
				85:6342-6346 (1988); Black et al., Virus	Other preferred indications include benign dysproliferative
				Genes 15(2):105-117 (1997); and	disorders and pre-neoplastic conditions, such as, for
				Belkowski et al., J Immunol 161(2):659-	example, hyperplasia, metaplasia, and/or dysplasia.
				665 (1998), the contents of each of which	Preferred indications include anemia, pancytopenia,
				are herein incorporated by reference in its	leukopenia, thrombocytopenia, acute lymphocytic anemia
				entirety. T cells that may be used	(ALL), plasmacytomas, multiple myeloma, arthritis,
				according to these assays are publicly	AIDS, granulomatous disease, inflammatory bowel
				available (e.g., through the ATCC).	disease, sepsis, neutropenia, neutrophilia, psoriasis,
				Exemplary human T cells that may be used	suppression of immune reactions to transplanted organs
				according to these assays include the	and tissues, hemophilia, hypercoagulation, diabetes
				JURKAT cell line, which is a suspension	mellitus, endocarditis, meningitis, Lyme Disease, and
				culture of leukemia cells that produce IL-2	asthma and allergy.
\dashv				when stimulated.	
423	HTEEW69	937	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and

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		·	antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4 cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	suppressing a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Tmmune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
423 HTEEW69	937	Activation of transcription through NFKB response element in immune cells (such as T-cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon,

			Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).	pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune
423 HTEEW69	937	Activation of transcription through NFKB response element in immune cells (such as B-cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Gri G, et al., Biol Chem, 273(11):6431-6438 (1998); Pyatt DW, et al., Cell Biol Toxicol 2000;16(1):41-51 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al., Immunology 90(3):45-460 (1997).	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Autoimmunity, Allergy and Asthma

				Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-	
				844 (1999), the contents of each of which	
				are herein incorporated by reference in its	
				entirety. Immune cells that may be used	
	-			according to these assays are publicly	
				available (e.g., through the AICC).	
				Exemplary immune cells that may be used	
				according to these assays include the Keh B-cell line.	
423 HTEEW69	W69	937	Upregulation of CD152	CD152 FMAT. CD152 (a.k.a. CTLA-4)	A highly preferred embodiment of the invention
			and activation of T cells	expression is restricted to activated T cells.	includes a method for activating T cells. An alternative
				CD152 is a negative regulator of T cell	highly preferred embodiment of the invention includes a
				proliferation. Reduced CD152 expression	fori
				has been linked to hyperproliferative and	T cells. A highly preferred embodiment of the
				autoimmune diseases. Overexpression of	invention includes a method for inhibiting T cell
				CD152 may lead to impaired	proliferation. An alternative highly preferred embodiment
				immunoresponses. Assays for	of the invention includes a method for stimulating T cell
				immunomodulatory proteins important in	proliferation. Highly preferred indications include
				the maintenance of T cell homeostasis and	blood disorders (e.g., as described below under "Immune
				expressed almost exclusively on CD4+ and	Activity", "Blood-Related Disorders", and/or
				CD8+ T cells are well known in the art and	"Cardiovascular Disorders"), Highly preferred indications
				may be used or routinely modified to	include autoimmune diseases (e.g., rheumatoid arthritis,
				assess the ability of polypeptides of the	systemic lupus erythematosis, multiple sclerosis and/or as
				invention (including antibodies and	described below), immunodeficiencies (e.g., as described
				agonists or antagonists of the invention) to	below), boosting a T cell-mediated immune response, and
				modulate the activation of T cells,	suppressing a T cell-mediated immune response.
				maintain T cell homeostasis, and/or	Highly preferred indications include neoplastic diseases
				mediate humoral or cell-mediated	(e.g., leukemia, lymphoma, and/or as described below
				immunity. Exemplary assays that test for	under "Hyperproliferative Disorders"). Additionally,
				immunomodulatory proteins evaluate the	highly preferred indications include neoplasms and
				upregulation of cell surface markers, such	cancers, such as, for example, leukemia, lymphoma,
				as CD152, and the activation of T cells.	melanoma, and prostate, breast, lung, colon, pancreatic,
				Such assays that may be used or routinely	esophageal, stomach, brain, liver and urinary cancer.
				modified to test immunomodulatory	Other preferred indications include benign dysproliferative
				activity of polypeptides of the invention	disorders and pre-neoplastic conditions, such as, for
				(including antibodies and agonists or	example, hyperplasia, metaplasia, and/or dysplasia.

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Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, inflammation and inflammatory disorders, and asthma and allergy. An additional preferred indication is infection (e.g., as described below under "Infectious Disease").	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Tmmune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and
antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); McCoy et al., Immunol Cell Biol 77(1):1-10 (1999); Oostervegal et al., Curr Opin Immunol 11(3):294-300 (1999); and Saito T, Curr Opin Immunol 10(3):313-321 (1998), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention)
	Activation of transcription through serum response element in immune cells (such as T-cells).
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			include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, ALDS, granulomatous disease, inflammatory bowel disease, neutropenia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below and at "Tafactions Disease.")
425 HTEGS11	939	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated

			activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
		4-14	invention (including antibodies and	immune response. Additional highly preferred indications
			agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
			include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
			Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
-			Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
			Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
			85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
			Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
			content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
-			incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
			cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
			assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
			the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
			may be used according to these assays	pre-neoplastic conditions, such as, for example,
			include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
			2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
			with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				anemia (ALL), plasmacytomas, multiple myeloma,
				Burkitt's lymphoma, arthritis, AIDS, granulomatous
		•		disease, inflammatory bowel disease, neutropenia,
				neutrophilia, psoriasis, suppression of immune reactions to
				transplanted organs and tissues, hemophilia,
-				hypercoagulation, diabetes mellitus, endocarditis,
				meningitis, Lyme Disease, cardiac reperfusion injury, and
				asthma and allergy. An additional preferred indication
				is infection (e.g., an infectious disease as described below
				under "Infectious Disease").
426 HTEHA56	940	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
		ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
		Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
			or differentiation are well known in the art	invention includes a method for inhibiting adipocyte
			and may be used or routinely modified to	proliferation. A highly preferred embodiment of the
			assess the ability of polypeptides of the	invention includes a method for stimulating adipocyte
			invention (including antibodies and	differentiation. An alternative highly preferred
	_		agonists or antagonists of the invention) to	Sa
			promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly

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	activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
•	assays for EKK kinase activity that may be used or routinely modified to test ERK	for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention
	kinase-induced activity of polypeptides of	o uo
	the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
	agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders")
	al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
	(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
	Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
	(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
	64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
	410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
	Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
	(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
	herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
-	entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
	be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
	publicly available (e.g., through the	described below under "Infectious Disease").
	ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
	that may be used according to these assays	additional highly preferred indication is a complication
	include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
	adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
	cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		"Cardiovascular Disorders" section below), dyslipidemia,
		endocrine disorders (as described in the "Endocrine
-		Disorders" section below), neuropathy, vision impairment
		(e.g., diabetic retinopathy and blindness), ulcers and

impaired wound heling, infection (e.g., infectious diseases and disoades and discutes as described in the "Infectious Diseases" section below (particularly of the unimary tract and skin). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications include with sopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include with a disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases of disorders. Preferred indications include neoplasms and cancer, such as Jymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include meanoma, prostate, lung, pancreatic, esophageal, stomach, ho ain, liver, and urinary cancer. Highly preferred indications include benign dyspoliferative disorders and pre-neoplasms, and or Adspoliferative disorders and pre-neoplasmic conditions, such as concerned indications include benign dyspoliferative disorders and pre-neoplasmic and or dysplasia.	HA56 940 Activation of Adipocyte Kinase assay. Kinase assay, for PI3 kinase Signalling an GSK-3 assays, for PI3 kinase signal transduction that regulate glucose metabolism and cell survival are well-known in the art and may be used or routinely modified to assess the ability of the invention includes a method for increasing adipocyte survival. A preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation includes a method for stimulating adipocyte proliferation.
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				associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include, hypertension, coronary artery disease, dyslipidemia, gallstones, osteoarthritis, degenerative arthritis, eating disorders, fibrosis, cachexia, and kidney diseases or disorders. Highly preferred indications include neoplasms and cancer, such as, lipoma, liposarcoma, lymphoma, leukemia and breast, colon, and kidney cancer. Additional highly preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and prenetaplasia, and/or dysplasia.
427 HTEHUS9	941	Calcium flux in chondrocytes	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux in chondrocytes include assays disclosed in: Asada S, et al., Inflamm Res, 50(1):19-23 (2001);	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Bone and Cartilage Diseases, including but not limited to Arthritis, Cartilige repair, Bone Repair, Osteoporosis, and related tumors including chondrosarcomas, chondroblastomas, and chondromas.

			Schwartz Z, et al., J Bone Miner Res, 6(7):709-718 (1991); Iannotti JP, et al., J Bone Joint Surg Am, 67(1): 113-120 (1985); Sullivan E., et al., Methods Mol Biol 1999; 114:125-133 (1999), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include	
427 HTEHU59	941	Activation of transcription through GAS response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic differences.

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				4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
428	HTEJD29	942	Stimulation of Calcium Flux in pancreatic beta cells.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Satin LS, et al., Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al., Cell Calcium 1989 Nov. Dec. 10(8):535-41	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with

	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
6(7):709-718 (1991); Iannotti JP, et al., J Bone Joint Surg Am, 67(1): 113-120 (1985); Sullivan E., et al., Methods Mol Biol 1999; 114:125-133 (1999), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include bovine chondrocytes.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E-antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may play a role in allergic disease and mast cell tumor survival. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity induced by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Masuda A, et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp
	Regulation of apoptosis of immune cells (such as mast cells).
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	is diabetes mel sation is a con attion is a con tic retinopath we (e.g., renal mid disorders section below e damage (e.g. plockage, hear ettic neuropatt ental confusic mic-hyperosm heart disease, ase, hypertens ders as describelow), dyslin the "Endocriathy, vision in the "Infectic of the urinary Dupuytren's hly preferred ociated with ociated
	erred indication is diabetes mellitus. hly preferred indication is a complication abetes (e.g., diabetic retinopathy, tidney disease (e.g., renal failure, or other diseases and disorders as Renal Disorders" section below), diabetic disease and nerve damage (e.g., due to hy), blood vessel blockage, heart disease, (e.g., due to diabetic neuropathy or kage), seizures, mental confusion, etotic hyperglycemic-hyperosmolar ular disease (e.g., heart disease, ular disease, and disorders as described in the Disorders" section below), dyslipidemia, ars (as described in the "Endocrine n below), neuropathy, vision impairment nopathy and blindness), ulcers and realing, infection (e.g., an infectious lers as described in the "Infectious lers as described in the "Infectious lers as described in the "Infectious abelow, especially of the urinary tract and el syndrome and Dupuytren's An additional highly preferred indication complications associated with obesity.
	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy) blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infection (e.g., an infectious diseases or disorders as described in the "Infectious biseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity.
	An ad associ diabet nephrodiabet descriped diabet stroke stroke blood drows coma athero stroke "Card athero stroke "Card and coma athero stroke "Card and coma athero stroke "Card and coma athero stroke (e.g., impain diseas bison contra is obe
Med, 192(8):1093-1103 (2000); Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	Assays for the regulation of transcription through the PEPCK promoter are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the PEPCK promoter in a reporter construct and regulate liver gluconeogenesis. Exemplary assays for regulation of transcription through the PEPCK promoter that may be used or routinely modified to test for PEPCK promoter activity (in hepatocytes) of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Lochhead et al., Diabetes 49(6):896-903 (2000); and Yeagley et al., J Biol Chem 275(23):17814-17820 (2000), the contents of each of which is herein incorporated by
5-1103 (200 3): 122-126 37(3): 209-3 37(3): 209-3 arlan, J Ath 80 (1996): t herein inco tirety. Imm rding to the (e.g., throu es). Exemp used accord ist cells such ine.	inition of the control of the contro
Med, 192(8):1093-1103 (2000);Lee et al., FEBS Lett 485(2-3): 122-126 (2000); Nor et al., J Vasc Res 37(3): 209-218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	Assays for the regulation of transcription through the PEPCK promoter are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the PEPCK promoter in a reporter construct and regulate liver gluconeogenesis. Exemplary assays for regulation of transcription through the PEPCK promoter that may be used or routinely modified to test for PEPCK promoter activity (in hepatocytes) of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 83:6342-6346 (1988); Lochhead et al., Diabetes 49(6):896-903 (2000); and Yeagley et al., J Biol Chem 275(23):17814-17820 (2000), the contents of each of which is herein incorporated by
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	Regulation of transcription through the PEPCK promoter in hepatocytes
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Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications associated with insulin resistance. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include glycogen storage disease (e.g., glycogenoses), hepatitis, gallstones, cirrhosis of the liver, degenerative or necrotic liver disease, alcoholic liver diseases, fibrosis, liver regeneration, metabolic disease, dyslipidemia and cholesterol metabolism, and hepatocarcinomas. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders (e.g., as described below under "Immune Activity"), infection (e.g., an infectious disease and/or disorder as described below under "Immune Activity"), and Neurological Diseases"), endocrine disorders (e.g., as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic
ht gain. Ac are complications Additions ers of the muscular dystro Addition and Addition ers of the muscular dystro Addition Addition Addition Addition Addition ycogen storage di tis, gallstones, cii tic liver disease, r regeneration, rr lesterol metabolis prs (e.g., as descri Cardiovascular Dr rders"), immune extiv and/or disorder a feases"). include neoplasti include neoplasti include benign d poplastic condition ma, prostate, brea dication is liver c include benign d oplastic condition metaplasia, and	A highly preferred indication is diabetes mellitus. idditional highly preferred indication is a complic ciated with diabetes (e.g., diabetic retinopathy, etic nephropathy, kidney disease (e.g., renal failu ropathy and/or other diseases and disorders a ribed in the "Renal Disorders" section below), dis
Additional highly preferred indications include weight lor alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein. Additional highly preferred indications include glycogen storage disease (e.g., glycogenoses), hepatitis, gallstones, cirrhosis of the liver diseases, fibrosis, liver regeneration, metabolic disease, dyslipidemia and cholesterol metabolism, and hepatocarcinomas. Highly preferred indication include blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders", immune disorders (e.g., as described below under "Immune Activity"), infection (an infectious disease and/or disorder as described below under "Endocrine Disorders"), and net disorders (e.g., as described below under "Hyperproliferative Disorders"), and Neurological Diseases"). Additional preferred indications include neoplasms and cancers, stas, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary can A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred indication is diabetes mellit An additional highly preferred indication is a comp associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal fai nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),
	An ass dia neg
reference in its entirety. Hepatocyte cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary liver hepatoma cells that may be used according to these assays include H4lle cells, which contain a tyrosine amino transferase that is inducible with glucocorticoids, insulin, or cAMP derivatives.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of
that may be used according to these assay are publicly available (e.g., through the ATCC) and/or may be routinely generate Exemplary liver hepatoma cells that may be used according to these assays include H4lle cells, which contain a tyrosine ami transferase that is inducible with glucocorticoids, insulin, or cAMP derivatives.	Assays for the regulation of viability a proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the abilit polypeptides of the invention (includi antibodies and agonists or antagonists
	Regulation of viability and proliferation of pancreatic beta cells.
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	HTGGM44
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the invention) to regulate viability and proliferation of pancreatic bear cells. For example, the Cell Titre-Cilo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonist or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonists of the invention) (including antibodies and agonists or antagonist or the assays include are a semi-adherent cell inc established from cells isolated from any every pancreatic cells that may be used according to these assays include are a semi-adherent cell inc established from cells isolated from any X-ray induced rat transplantable insulinoma. These cells retain	beta cells including glucose inductore insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	nsulin
		Stimulation of insuli secretion from
		947
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described in the "Renal Disorders" section below), diabetic stroke, and other diseases and disorders as described in the Diseases" section below, especially of the urinary tract and Aditional diabetic neuropathy), blood vessel blockage, heart disease, Disorders" section below), neuropathy, vision impairment indication is obesity and/or complications associated with neuropathy, nerve disease and nerve damage (e.g., due to "Cardiovascular Disorders" section below), dyslipidemia, highly preferred indications are complications associated obesity. Additional highly preferred indications include diabetic nephropathy, kidney disease (e.g., renal failure, impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious stroke, impotence (e.g., due to diabetic neuropathy or atherosclerosis, microvascular disease, hypertension, drowsiness, nonketotic hyperglycemic-hyperosmolar (e.g., diabetic retinopathy and blindness), ulcers and endocrine disorders (as described in the "Endocrine nephropathy and/or other diseases and disorders as blood vessel blockage), seizures, mental confusion, An additional highly preferred coma, cardiovascular disease (e.g., heart disease, skin), carpal tunnel syndrome and Dupuytren's weight loss or alternatively, weight gain. with insulin resistance. contracture). Kim, K.H., et al., FEBS Lett, 377(2):237-9 ine established from cells isolated from an of polypeptides of the invention (including nsulin secretion. References: Asfari et al. according to these assays include rat INS-1 entirety. Pancreatic cells that may be used characteristics typical of native pancreatic available (e.g., through the ATCC) and/or cells. INS-1 cells are a semi-adherent cell insulin antibodies. Insulin secretion from the invention) include assays disclosed in: (1995); and, Miraglia S et. al., Journal of secretion. For example, insulin secretion antibodies and agonists or antagonists of modified to test for stimulation of insulin antibodies and agonists or antagonists of Ahren, B., et al., Am J Physiol, 277(4 Pt polypeptides of the invention (including proteins/peptides, and disregulation is a Endocrinology, 138(9):3735-40 (1997); (1999), the contents of each of which is may be routinely generated. Exemplary key component in diabetes. Exemplary herein incorporated by reference in its beta cells including glucose inducible pancreatic beta cells is upregulated by according to these assays are publicly assays that may be used or routinely is measured by FMAT using anti-rat Biomolecular Screening, 4:193-204 secretion (from pancreatic cells) by 2):R959-66 (1999); Li, M., et al., the invention) to stimulate insulin pancreatic cells that may be used X-ray induced rat transplantable insulinoma. These cells retain glucose and also by certain

				Endocrinology 1992 130:167.	
434	HTLAP64	948	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
			-	(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,

				meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
435 HTLBT80	949	Activation of Adipocyte ERK Signaling Pathway	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Le Marchand-Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) adipocyte activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes. Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders"). Highly preferred indications also include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural
			entirety. Mouse adipocyte cells that may be used according to these assays are publicly available (e.g., through the	disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), and infection (e.g., as described below under "Infectious Disease").
			ATCC). Exemplary mouse adipocyte cells that may be used according to these assays include 3T3-L1 cells. 3T3-L1 is an	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy,
			adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast	diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as

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	cells developed through clonal isolation	described in the "Renal Disorders" section below). diabetic
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,
		stroke, and other diseases and disorders as described in the
		"Cardiovascular Disorders" section below), dyslipidemia,
		endocrine disorders (as described in the "Endocrine
		Disorders" section below), neuropathy, vision impairment
		(e.g., diabetic retinopathy and blindness), ulcers and
-		impaired wound healing, infection (e.g., infectious
		diseases and disorders as described in the "Infectious
		Diseases" section below (particularly of the urinary tract
		and skin). An additional highly preferred indication is
		obesity and/or complications associated with obesity.
		Additional highly preferred indications include weight loss
		or alternatively, weight gain. Additional highly
		ons are
		insulin resistance. Additional highly preferred
		indications are disorders of the musculoskeletal systems
		hies
		described herein. Additional highly preferred
		indications include, hypertension, coronary artery disease,
		dyslipidemia, gallstones, osteoarthritis, degenerative
		arthritis, eating disorders, fibrosis, cachexia, and kidney
		diseases or disorders. Preferred indications include
		neoplasms and cancer, such as, lymphoma, leukemia and
		breast, colon, and kidney cancer. Additional preferred
		indications include melanoma, prostate, lung, pancreatic,
		esophageal, stomach, brain, liver, and urinary cancer.
-		Highly preferred indications include lipomas and
		liposarcomas. Other preferred indications include benign
		dysproliferative disorders and pre-neoplastic conditions,
		such as, for example, hyperplasia, metaplasia, and/or

dysplasia.		Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Autoimmunity, Allergy and Asthma.
	Assays for the activation of transcription through the EGR response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate EGR transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the EGR response element that may be used or routinely modified to test EGR response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Richards JD, et al., J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp Med, 188(12):2215-2224 (1998); and, Newton, JS, et al., Eur J Immunol 1996 Apr;26(4):811-816 (1996), the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary immune cells that may be used according to these assays include the Raji B-cell line.	Assays for the activation of transcription through the EGR response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate EGR transcription factors and modulate
	Activation of transcription through the EGR (Early Growth Response) element in immune cells (such as B-cells).	Activation of transcription through the EGR (Early Growth Response) element in immune cells (such as B-cells).
	949	949
	HTLBT80	HTLBT80
	435	435

		÷	Pyatt DW, et al., Cell Biol 10xicol 2000;16(1):41-51 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al, Immunology 90(3):455-460 (1997); Aramburau et al., J Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary immune cells that may be used according to these assays include the Reh B-cell line.	
436 HTLDA84	020	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell mediate immunity.	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. Additional preferred indications include

e the erferon ff T or or ding tts of closed closed ach" is z et al., i					Exemplary assays that test for	indications include neonlastic diseases (e.g. leukemia
production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention (including antibodies and agonists or antagonists of the invention include the assays disclosed in Miraglia et al., 18 Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach," Chapter 6:138-160 (2000); Gonzalez et al., Tolin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann WY Acad Sci 856:22-32 (1998); Bolliau et al., Ann WY Acad Sc					imminomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention include the assays disclosed in Miraglia et al., 1 Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:136-160 (2000); Goraelez et al., 1 Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Ann Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human which herein or otherwise shown in the art. Human T cells are primary human wherein or otherwise shown in the art. Human T cells are primary human wherein or otherwise shown in the art. Human T cells are primary human wherein or otherwise shown in the art. Human T cells are primary human wherein or otherwise shown in the art. Human T cells are primary human wherein or otherwise and cuts of cells and act or immunomodulatory factors. HTLDN29 951 Production of MCP-1 IFMAT. Assays for a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely.					production of cytokines. such as Interferon	"Hyperproliferative Disorders"). Highly preferred
cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention fincluding antibodies and agonists or antagonists of the invention include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boelm et al., Ann NY Acad Sci 856:22-32 (1998); Boelm et al., Ann NY Acad Sci 856:22-32 (1998); Boelm et al., Ann Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunoomodulatory factors. HTLDN29 951 Production of MCP-1 Immunoomodulatory proteins that are produced by a large variety of cells and act to influence chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely.					gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4.193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-166 (2000); Conzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billian et al., Ann NY Acad Sci 886:22-33 (1998); Boehne et al., Ann Rev Immunol 15:749-795 (1997), and Rheumantology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirey. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are mell known in the art and may be used or routinely.					cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention include the assays disclosed in Miraglia et al., H Biomolecular Screening 4:193-204 (1999), Rowland et al., "Lymphocytes: a practical approach" Chapter ci. 18-160 (2000), Gonzalez et al., J Clin Lab Anal 8(5):25-233 (1995), Billiau et al., Ann NY Acad Sci 856:22-32 (1998), Boehm et al., Ann NY Acad Sci 856:22-32 (1998), Boehm et al., Ann NR Acad Sci 856:22-32 (1998), Boehm et al., Ann NR Acad Sci 86:22-32 (1998), Boehm et al., Ann Rev Immunol 15:749-795 (1997), and Rheumatology Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells and sciolated using techniques disclosed herein or otherwises known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemologias and 2 realis are well known in the art and may be used or routinely.					routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., 1 Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" (Chapter 6:138-160 (2020); Gonzalez et al., 1 Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Ann Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be pracativated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely.					immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that may be used according to these herein or OrD8. These cells mediate humoral or CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 MCP-1 FMAT. Assays for immunomodulatory proteins that are production of monocytes and T cells are well known in the art and may be used or routinely or					polypeptides of the invention (including	include benign dysproliferative disorders and pre-
in Miraglia et al., 1 Biomolecular Screening 4: 193-204 (1999), Rowland et al., "Lymphocytes: a practical approach" (Chapter 6: 138-160 (2000); Gonzalez et al., 1 Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Belliau et al., Ann NY Acad Sci 856:22-32 (1998); Belliau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Ann NR ver Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human hymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely				-	antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Ann Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. MCP-1 FMAT. Assays for immunomodulatory factors. MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boelm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated to enhance responsiveness to immunomodulatory factors. MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boelme et al., Ann Rev Immunol 15.749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. MCP-1 FMAT. Assays for immunomodulatory colls and act immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
Chapter 6.138-160 (2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 MCP-1 FMAT. Assays for immunomodulatory factors. Production of MCP-1 monocytes and zetles and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely.					al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
J Clin Lab Anal 8(5):225-233 (1995); Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HILDN29 951 Production of MCP-1 immunomodulatory factors. MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
Billiau et al., Ann NY Acad Sci 856:22-32 (1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are prinary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 MCP-1 RMAT. Assays for immunomodulatory factors. MCP-1 FMAT. Assays for immunomodulatory to feells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
(1998); Boehm et al., Annu Rev Immunol 15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 MAP. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
15:749-795 (1997), and Rheumatology (Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 immunomodulatory factors. MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
Oxford) 38(3):214-20 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
hy reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					of each of which are herein incorporated	
HTLDN29 HATLDN29 HATLDN2					by reference in its entirety. Human T cells	
may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					that may be used according to these assays	
Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					may be isolated using techniques disclosed	
Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					herein or otherwise known in the art.	
lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					Human T cells are primary human	
express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					lymphocytes that mature in the thymus and	
HTLDN29 951 Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be preactivated to enhance responsiveness to immunomodulatory factors. HTLDN29 951 MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					express a T Cell receptor and CD3, CD4,	
HTLDN29 951 Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be preactivated immunomy and may be used or routinely					or CD8. These cells mediate humoral or	
HTLDN29 951 Production of MCP-1 MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					cell-mediated immunity and may be	
HTLDN29 951 Production of MCP-1 MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely	•				preactivated to enhance responsiveness to	
HTLDN29 951 Production of MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely					immunomodulatory factors.	
	437	HTLDN29	951	Production of MCP-1	MCP-1 FMAT. Assays for	A highly preferred embodiment of the invention
	•				immunomodulatory proteins that are	includes a method for stimulating (e.g., increasing) MCP-1
					produced by a large variety of cells and act	production. An alternative highly preferred embodiment of
					to induce chemotaxis and activation of	the invention includes a method for inhibiting (e.g.,
					monocytes and T cells are well known in	reducing) MCP-1 production. A highly preferred
					the art and may be used or routinely	indication is infection (e.g., an infectious disease as

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				modified to assess the ability of	described below under "Infectious Disease"). Additional
				polypeptides of the invention (including	highly preferred indications include inflammation and
				antibodies and agonists or antagonists of	inflammatory disorders. Preferred indications include
				the invention) to mediate	blood disorders (e.g., as described below under "Immune
				immunomodulation, induce chemotaxis,	Activity", "Blood-Related Disorders", and/or
				and modulate immune cell activation.	"Cardiovascular Disorders"). Highly preferred indications
				Exemplary assays that test for	include autoimmune diseases (e.g., rheumatoid arthritis,
				immunomodulatory proteins evaluate the	systemic lupus erythematosis, multiple sclerosis and/or as
				production of cell surface markers, such as	described below) and immunodeficiencies (e.g., as
				monocyte chemoattractant protein (MCP),	described below). Preferred indications also include
				and the activation of monocytes and T	anemia, pancytopenia, leukopenia, thrombocytopenia,
				cells. Such assays that may be used or	Hodgkin's disease, acute lymphocytic anemia (ALL),
				routinely modified to test	plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				immunomodulatory and diffferentiation	arthritis, AIDS, granulomatous disease, inflammatory
				activity of polypeptides of the invention	bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
				(including antibodies and agonists or	suppression of immune reactions to transplanted organs
				antagonists of the invention) include	and tissues, hemophilia, hypercoagulation, diabetes
				assays disclosed in Miraglia et al., J	mellitus, endocarditis, meningitis (bacterial and viral),
				Biomolecular Screening 4:193-204(1999);	Lyme Disease, asthma, and allergy Preferred indications
				Rowland et al., "Lymphocytes: a practical	also include neoplastic diseases (e.g., leukemia,
				approach" Chapter 6:138-160 (2000);	lymphoma, and/or as described below under
				Satthaporn and Eremin, J R Coll Surg	"Hyperproliferative Disorders"). Highly preferred
				Ednb 45(1):9-19 (2001); and Verhasselt et	indications include neoplasms and cancers, such as,
				al., J Immunol 158:2919-2925 (1997), the	leukemia, lymphoma, prostate, breast, lung, colon,
				contents of each of which are herein	pancreatic, esophageal, stomach, brain, liver, and urinary
				incorporated by reference in its entirety.	cancer. Other preferred indications include benign
				Human dendritic cells that may be used	dysproliferative disorders and pre-neoplastic conditions,
				according to these assays may be isolated	such as, for example, hyperplasia, metaplasia, and/or
				using techniques disclosed herein or	dysplasia.
				otherwise known in the art. Human	
				dendritic cells are antigen presenting cells	
				in suspension culture, which, when	
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation	
				and functional activities.	
437	HTLDN29	951	Production of MIP1alpha	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by	A highly preferred embodiment of the invention includes a method for stimulating MIP a production. An

	activated dendritic cells that upregulate	alternative highly preferred embodiment of the invention
	monocyte/macrophage and T cell	includes a method for inhibiting (e.g., reducing) MIP1a
	chemotaxis are well known in the art and	production. A highly preferred indication is infection
	may be used or routinely modified to	(e.g., an infectious disease as described below under
	assess the ability of polypeptides of the	"Infectious Disease"). Preferred indications include
	invention (including antibodies and	blood disorders (e.g., as described below under "Immune
-	agonists or antagonists of the invention) to	Activity", "Blood-Related Disorders", and/or
	mediate immunomodulation, modulate	"Cardiovascular Disorders"). Highly preferred indications
	chemotaxis, and modulate T cell	include autoimmune diseases (e.g., rheumatoid arthritis,
	differentiation. Exemplary assays that test	systemic lupus erythematosis, multiple sclerosis and/or as
	for immunomodulatory proteins evaluate	described below) and immunodeficiencies (e.g., as
	the production of chemokines, such as	described below). Additional highly preferred indications
	macrophage inflammatory protein 1 alpha	include inflammation and inflammatory disorders.
	(MIP-1a), and the activation of	Preferred indications also include anemia, pancytopenia,
	monocytes/macrophages and T cells. Such	leukopenia, thrombocytopenia, Hodgkin's disease, acute
	assays that may be used or routinely	lymphocytic anemia (ALL), plasmacytomas, multiple
	modified to test immunomodulatory and	myeloma, Burkitt's lymphoma, arthritis, AIDS,
	chemotaxis activity of polypeptides of the	granulomatous disease, inflammatory bowel disease,
	invention (including antibodies and	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
	agonists or antagonists of the invention)	immune reactions to transplanted organs and tissues,
	include assays disclosed in Miraglia et al.,	hemophilia, hypercoagulation, diabetes mellitus,
	J Biomolecular Screening 4:193-	endocarditis, meningitis, Lyme Disease, asthma, and
	204(1999); Rowland et al., "Lymphocytes:	allergy. Preferred indications also include neoplastic
	a practical approach" Chapter 6:138-160	diseases (e.g., leukemia, lymphoma, and/or as described
	(2000); Satthaporn and Eremin, J R Coll	below under "Hyperproliferative Disorders"). Highly
	Surg Ednb 45(1):9-19 (2001); Drakes et	preferred indications include neoplasms and cancers, such
	al., Transp Immunol 8(1):17-29 (2000);	as, leukemia, lymphoma, prostate, breast, lung, colon,
	Verhasselt et al., J Immunol 158:2919-	pancreatic, esophageal, stomach, brain, liver, and urinary
	2925 (1997); and Nardelli et al., J Leukoc	cancer. Other preferred indications include benign
	Biol 65:822-828 (1999), the contents of	dysproliferative disorders and pre-neoplastic conditions,
	each of which are herein incorporated by	such as, for example, hyperplasia, metaplasia, and/or
	reference in its entirety. Human dendritic	dysplasia.
	cells that may be used according to these	
	assays may be isolated using techniques	
	disclosed herein or otherwise known in the	
	art. Human dendritic cells are antigen	
	presenting cells in suspension culture,	

	A highly preferred indication is diabetes melitius. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. A highly preferred indications are complications associated with insulin resistance.
which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent cell viability assay measures the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. Exemplary assays that may be used or routinely modified to test regulation of viability and proliferation of pancreatic beta cells by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Friedrichsen BN, et al., Mol Endocrinol, 15(1):136-48 (2001); Huotari MA, et al., Endocrinology, 139(4):1494-9 (1998); Hugl SR, et al., J Biol Chem 1998 Jul 10;273(28):17771-9 (1998), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an
	Regulation of viability and proliferation of pancreatic beta cells.
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X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Proliferation, differentiation, and/or cytokine production in immune cells (such as T-cells).	Production of IL-6
Mc Millione	952	952
	HTLDU78	HTLDU78
	438	438

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outotovic T calle Deremilated evaraction	indication is the ctimilation or enhancement of micosal
 of II6 has been linked to autoimmune	immunity. Highly preferred indications include blood
disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
 Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
 differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
 a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
 cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
or routinely modified to assess the ability	preferred indications also include boosting a B cell-
of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
the invention) to mediate	indications include inflammation and inflammatory
immunomodulation and differentiation and	disorders. Additional highly preferred indications include
modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
 each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
 reference in its entirety. Human dendritic	==
cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
 assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
disclosed herein or otherwise known in the	described below under "Infectious Disease").

				art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities	
439	HTLEC82	. 953	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease").
				the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention	Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6347 6346 (1988); Dellohan et al.	also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary
				63:0342-0340 (1986); Kellanan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986- 4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety.	dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma,
į				Human T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is an IL-2 and IL-4 responsive suspensionculture cell line.	Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.

Preferred embodiments of the invention include using	polypeptides of the invention (or antibodies, agonists, or	antagonists thereof) in detection, diagnosis, prevention,	and/or treatment of asthma, allergy, hypersensitivity and	inflammation.																																
Caspase Apoptosis. Assays for caspase	apoptosis are well known in the art and	may be used or routinely modified to	assess the ability of polypeptides of the	invention (including antibodies and	agonists or antagonists of the invention) to	regulate caspase protease-mediated	apoptosis in immune cells (such as, for	example, in mast cells). Mast cells are	found in connective and mucosal tissues	throughout the body, and their activation	via immunoglobulin E -antigen, promoted	by T helper cell type 2 cytokines, is an	important component of allergic disease.	Dysregulation of mast cell apoptosis may	play a role in allergic disease and mast cell	tumor survival. Exemplary assays for	caspase apoptosis that may be used or	routinely modified to test capase apoptosis	activity induced by polypeptides of the	invention (including antibodies and	agonists or antagonists of the invention)	include the assays disclosed in: Masuda A,	et al., J Biol Chem, 276(28):26107-26113	(2001); Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103 (2000);Lee et al.,	FEBS Lett 485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-218 (2000);	and Karsan and Harlan, J Atheroscler	Thromb 3(2): 75-80 (1996); the contents of	each of which are herein incorporated by	reference in its entirety. Immune cells that	may be used according to these assays are	publicly available (e.g., through	commercial sources). Exemplary immune	cells that may be used according to these	assays include mast cells such as the HMC
Regulation of apoptosis	of immune cells (such	as mast cells).																																		
954														•																						
HTLEM16																																				
440																																				

				human mast cell line.	
440	HTLEM16	954	Activation of	Kinase assay. JNK and p38 kinase assays	A highly preferred embodiment of the invention
			Endothelial Cell p38 or	for signal transduction that regulate cell	includes a method for stimulating endothelial cell growth.
			JNK Signaling	proliferation, activation, or apoptosis are	An alternative highly preferred embodiment of the
	<u>. </u>		Pathway.	well known in the art and may be used or	invention includes a method for inhibiting endothelial cell
				routinely modified to assess the ability of	growth. A highly preferred embodiment of the
				polypeptides of the invention (including	invention includes a method for stimulating endothelial
				antibodies and agonists or antagonists of	cell proliferation. An alternative highly preferred
				the invention) to promote or inhibit cell	embodiment of the invention includes a method for
				proliferation, activation, and apoptosis.	inhibiting endothelial cell proliferation. A highly
				Exemplary assays for JNK and p38 kinase	includ
				activity that may be used or routinely	for stimulating apoptosis of endothelial cells. An
				modified to test JNK and p38 kinase-	alternative highly preferred embodiment of the invention
				induced activity of polypeptides of the	includes a method for inhibiting (e.g., decreasing)
				invention (including antibodies and	apoptosis of endothelial cells. A highly preferred
				agonists or antagonists of the invention)	embodiment of the invention includes a method for
				include the assays disclosed in Forrer et	stimulating (e.g., increasing) endothelial cell activation.
				al., Biol Chem 379(8-9):1101-1110	An alternative highly preferred embodiment of the
				(1998); Gupta et al., Exp Cell Res 247(2):	invention includes a method for inhibiting (e.g.,
				495-504 (1999); Kyriakis JM, Biochem	decreasing) the activation of and/or inactivating
				Soc Symp 64:29-48 (1999); Chang and	endothelial cells. A highly preferred embodiment of
				Karin, Nature 410(6824):37-40 (2001);	the invention includes a method for stimulating
				and Cobb MH, Prog Biophys Mol Biol	angiogenisis. An alternative highly preferred embodiment
				71(3-4):479-500 (1999); the contents of	.=
				each of which are herein incorporated by	angiogenesis. A highly preferred embodiment of the
				reference in its entirety. Endothelial cells	invention includes a method for reducing cardiac
				that may be used according to these assays	hypertrophy. An alternative highly preferred embodiment
				are publicly available (e.g., through the	of the invention includes a method for inducing cardiac
				ATCC). Exemplary endothelial cells that	hypertrophy. Highly preferred indications include
				may be used according to these assays	neoplastic diseases (e.g., as described below under
				include human umbilical vein endothelial	"Hyperproliferative Disorders"), and disorders of the
				cells (HUVEC), which are endothelial	cardiovascular system (e.g., heart disease, congestive heart
				cells which line venous blood vessels, and	failure, hypertension, aortic stenosis, cardiomyopathy,
				are involved in functions that include, but	valvular regurgitation, left ventricular dysfunction,
				are not limited to, angiogenesis, vascular	atherosclerosis and atherosclerotic vascular disease,
				permeability, vascular tone, and immune	diabetic nephropathy, intracardiac shunt, cardiac
				cell extravasation.	hypertrophy, myocardial infarction, chronic hemodynamic

		overload, and/or as described below under
		"Cardiovascular Disorders"). Highly preferred indications
		include cardiovascular endothelial and/or angiogenic
		disorders (e.g. systemic disorders that affect vessels such
		disolucis (c.g., systemic disolucis mai anice vessers such
		as diabetes meliitus, as well as diseases of the vessels
		themselves, such as of the arteries, capillaries, veins and/or
		lymphatics). Highly preferred are indications that
		stimulate angiogenesis and/or cardiovascularization.
		Highly preferred are indications that inhibit angiogenesis
		and/or cardiovascularization. Highly preferred
		- 55
		tumors, leukemias, and Kaposi's sarcoma, and retinal
		disorders. Highly preferred indications include neoplasms
		and cancer, such as, Kaposi's sarcoma, hemangioma
		(capillary and cavernous). glomus tumors, telangiectasia.
		hacillary anoiomatosis hemanoioendothelioma
		cucinally anglomatories, inclinating controlling,
		angiosarcoma, naemangiopericytoma, lympnangioma,
		lymphangiosarcoma. Highly preferred indications also
		include cancers such as, prostate, breast, lung, colon,
		pancreatic, esophageal, stomach, brain, liver, and urinary
		cancer. Preferred indications include benign
		dysproliferative disorders and pre-neoplastic conditions,
		such as, for example, hyperplasia, metaplasia, and/or
		dysplasia. Highly preferred indications also include
		arterial disease, such as, atherosclerosis, hypertension,
		coronary artery disease, inflammatory vasculitides,
		Reynaud's disease and Reynaud's phenomenom,
		aneurysms, restenosis; venous and lymphatic disorders
		such as thrombophlebitis, lymphangitis, and lymphedema;
		and other vascular disorders such as peripheral vascular
		disease, and cancer. Highly preferred indications also
		include trauma such as wounds, burns, and injured tissue
		(e.g., vascular injury such as, injury resulting from balloon
		angioplasty, and atheroschlerotic lesions), implant
		fixation, scarring, ischemia reperfusion injury, rheumatoid
		arthritis, cerebrovascular disease, renal diseases such as
		acute renal failure, and osteoporosis. Additional highly

				assays include microvascular endothelial cells (MVEC).	
442	HTLFA13	926	Regulation of viability and proliferation of	Assays for the regulation of viability and proliferation of cells in vitro are well-	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication
			pancreatic beta cells.	known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
				routhery mounted to assess the ability of polypeptides of the invention (including	niabetic nephropathy, Kiuney disease (e.g., renarranne), nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to regulate viability and	neuropathy, nerve disease and nerve damage (e.g., due to
				proliferation of pancreatic beta cells. For	diabetic neuropathy), blood vessel blockage, heart disease, stroke importance (e.g. due to diabetic neuropathy or
				cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion,
				viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
				quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
				signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
				active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
				used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
				regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
				pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
				invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
				agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
				include assays disclosed in: Friedrichsen	diseases and disorders as described in the "Infectious
				BN, et al., Mol Endocrinol, 15(1):136-48	Diseases" section below, especially of the urinary tract and
				(2001); Huotari MA, et al., Endocrinology,	tunne
				139(4):1494-9 (1998); Hugl SR, et al., J	contracture). An additional highly preferred
				Biol Chem 1998 Jul 10;273(28):17771-9	indication is obesity and/or complications associated with
				(1998), the contents of each of which is	cations i
				herein incorporated by reference in its	weight loss or alternatively, weight gain. Aditional
				entirety. Pancreatic cells that may be used	highly preferred indications are complications associated
				according to these assays are publicly	with insulin resistance.
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	

				insulinoma These cells retain	
				characteristics tynical of native nancreatic	
				heta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
443	HTLFI73	156	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
			alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
				activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred
				smooth muscle, and other cell types that	embodiment of the invention includes a method for
				exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
				well known in the art and may be used or	as described below under "Immune Activity", "Blood-
				routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
				polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
				antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				the invention) to mediate	Crohn's disease, multiple sclerosis and/or as described
				immunomodulation, modulate	below), immunodeficiencies (e.g., as described below),
				inflammation and cytotoxicity. Exemplary	boosting a T cell-mediated immune response, and
				assays that test for immunomodulatory	suppressing a T cell-mediated immune response.
				proteins evaluate the production of	Additional highly preferred indications include
				cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
				alpha (TNFa), and the induction or	joint damage in patients with rheumatoid arthritis. An
				inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
				response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
				routinely modified to test	leukemia, lymphoma, and/or as described below under
				immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
				polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
				antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
				the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
				Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
				4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
				"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
				Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
				al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
	-			(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,

				Nardelli et al J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
				(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
				herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
				entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
				be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
				isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
				or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
				dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
				in suspension culture, which, when	Disease").
	•			activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation	
444	HTLGI89	958	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
			Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
				example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
				measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
				have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
				calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
				extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
				can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,
				activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
				pathways and alterations in cell functions.	stroke, and other diseases and disorders as described in the
				Exemplary assays that may be used or	"Cardiovascular Disorders" section below), dyslipidemia,
				routinely modified to measure calcium flux	endocrine disorders (as described in the "Endocrine
				by polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
_				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Satin LS, et al., Endocrinology,	diseases and disorders as described in the "Infectious
				136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
				al., Endocrinology, 136(7):2960-6 (1995);	skin), carpal tunnel syndrome and Dupuytren's
				Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
				3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
				Cell Calcium 1989 Nov-Dec;10(8):535-41	obesity. Additional highly preferred indications include

				. 1 . 1 . 2	
				(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
,				according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
			•	pancreatic cells that may be used	
				according to these assays include HITT15	
				Cells. HITT15 are an adherent epithelial	
				cell line established from Syrian hamster	
				islet cells transformed with SV40. These	
				cells express glucagon, somatostatin, and	
				glucocorticoid receptors. The cells secrete	
				insulin, which is stimulated by glucose and	
				glucagon and suppressed by somatostatin	
				or glucocorticoids. ATTC# CRL-1777	
				Refs: Lord and Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc. Natl. Acad.	
				Sci. USA 78: 4339-4343, 1981.	
445	HTLIF11	959	Protection from	Caspase Apoptosis Rescue. Assays for	A highly preferred embodiment of the invention
			Endothelial Cell	caspase apoptosis rescue are well known in	includes a method for stimulating endothelial cell growth.
			Apoptosis.	the art and may be used or routinely	An alternative highly preferred embodiment of the
			•	modified to assess the ability of the	invention includes a method for inhibiting endothelial cell
				polypeptides of the invention (including	growth. A highly preferred embodiment of the
				antibodies and agonists or antagonists of	invention includes a method for stimulating endothelial
-				the invention) to inhibit caspase protease-	cell proliferation. An alternative highly preferred
				mediated apoptosis. Exemplary assays for	me
				caspase apoptosis that may be used or	inhibiting endothelial cell proliferation. A highly
				routinely modified to test caspase	preferred embodiment of the invention includes a method
				apoptosis rescue of polypeptides of the	for stimulating endothelial cell growth. An alternative
				invention (including antibodies and	highly preferred embodiment of the invention includes a
				agonists or antagonists of the invention)	method for inhibiting endothelial cell growth. A
				include the assays disclosed in Romeo et	highly preferred embodiment of the invention includes a
				al., Cardiovasc Res 45(3): 788-794 (2000);	method for stimulating apoptosis of endothelial cells. An
				Messmer et al., Br J Pharmacol 127(7):	alternative highly preferred embodiment of the invention
· •				1633-1640 (1999); and J Atheroscler	includes a method for inhibiting (e.g., decreasing)
				Thromb 3(2): 75-80 (1996); the contents of	apoptosis of endothelial cells. A highly preferred

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بيط أيمهم ميسي مرمية سينسيما مسم مان تطيب كم علميم	ambodimont of the invantion included a method for
	בוווססתווובווו סו מוכ ווועבוווסוו וווכותתכט מ וווכמוסת זסו
reference in its entirety. Endothelial cells	stimulating angiogenisis. An alternative highly preferred
 that may be used according to these assays	embodiment of the invention includes a method for
are publicly available (e.g., through	inhibiting angiogenesis. A highly preferred
commercial sources). Exemplary	embodiment of the invention includes a method for
endothelial cells that may be used	reducing cardiac hypertrophy. An alternative highly
according to these assays include bovine	preferred embodiment of the invention includes a method
 aortic endothelial cells (bAEC), which are	for inducing cardiac hypertrophy. Highly preferred
an example of endothelial cells which line	indications include neoplastic diseases (e.g., as described
blood vessels and are involved in functions	below under "Hyperproliferative Disorders"), and
that include, but are not limited to,	disorders of the cardiovascular system (e.g., heart disease,
angiogenesis, vascular permeability,	congestive heart failure, hypertension, aortic stenosis,
vascular tone, and immune cell	cardiomyopathy, valvular regurgitation, left ventricular
extravasation.	dysfunction, atherosclerosis and atherosclerotic vascular
	disease, diabetic nephropathy, intracardiac shunt, cardiac
 	hypertrophy, myocardial infarction, chronic hemodynamic
	overload, and/or as described below under
	"Cardiovascular Disorders"). Highly preferred
	indications include cardiovascular, endothelial and/or
	angiogenic disorders (e.g., systemic disorders that affect
	vessels such as diabetes mellitus, as well as diseases of the
	vessels themselves, such as of the arteries, capillaries,
	veins and/or lymphatics). Highly preferred are indications
	that stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms
	and cancer, such as, Kaposi's sarcoma, hemangioma
	(capillary and cavernous), glomus tumors, telangiectasia,
	bacillary angiomatosis, hemangioendothelioma,
	angiosarcoma, haemangiopericytoma, lymphangioma,
	lymphangiosarcoma. Highly preferred indications also
 	include cancers such as, prostate, breast, lung, colon,
	pancreatic, esophageal, stomach, brain, liver, and urinary
	cancer. Preferred indications include benign

					dysproliferative disorders and pre-neoplastic conditions,
					such as, for example, hyperplasia, metaplasia, and/or
					dysplasia. Highly preferred indications also include
					arterial disease, such as, atherosclerosis, hypertension,
					coronary artery disease, inflammatory vasculitides,
					Reynaud's disease and Reynaud's phenomenom,
					aneurysms, restenosis; venous and lymphatic disorders
					such as thrombophlebitis, lymphangitis, and lymphedema;
					and other vascular disorders such as peripheral vascular
					disease, and cancer. Highly preferred indications also
					include trauma such as wounds, burns, and injured tissue
					(e.g., vascular injury such as, injury resulting from balloon
					angioplasty, and atheroschlerotic lesions), implant
					fixation, scarring, ischemia reperfusion injury, rheumatoid
					arthritis, cerebrovascular disease, renal diseases such as
					acute renal failure, and osteoporosis. Additional highly
					preferred indications include stroke, graft rejection,
					diabetic or other retinopathies, thrombotic and coagulative
					disorders, vascularitis, lymph angiogenesis, sexual
				•	disorders, age-related macular degeneration, and treatment
					/prevention of endometriosis and related conditions.
					Additional highly preferred indications include fibromas,
					heart disease, cardiac arrest, heart valve disease, and
					vascular disease. Preferred indications include blood
					disorders (e.g., as described below under "Immune
					Activity", "Blood-Related Disorders", and/or
					"Cardiovascular Disorders"). Preferred indications include
					autoimmune diseases (e.g., rheumatoid arthritis, systemic
					lupus erythematosis, multiple sclerosis and/or as described
					below) and immunodeficiencies (e.g., as described below).
					Additional preferred indications include inflammation and
					inflammatory disorders (such as acute and chronic
					inflammatory diseases, e.g., inflammatory bowel disease
					and Crohn's disease), and pain management.
446	HTLIF12	096	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred

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			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
	_			the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
_				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
				may be used according to these assays are	include anemia, pancytopenia, leukopenia,
				publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
				ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
				used according to these assays include the	granulomatous disease, inflammatory bowel disease,
				CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
				cells.	hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
447	HTLIF12	961	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
				Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			III IIIIIIIIII COIIS (SACII	KINDWIL III UIC ALL AIN IIIAY DC USCU OI	muications include heoptasins and cancers, such as, for

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			as T-rells)	routinely modified to assess the ability of	example lenkemia lymphoma (e.g. T cell lymphoma.
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications'
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
				may be used according to these assays are	include anemia, pancytopenia, leukopenia,
				publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
				ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
				used according to these assays include the	granulomatous disease, inflammatory bowel disease,
				CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
				cells.	hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
448	HTLIF12	962	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
				Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as I-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., I cell lymphoma,

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				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
			-	the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
				may be used according to these assays are	include anemia, pancytopenia, leukopenia,
				publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
				ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
				used according to these assays include the	granulomatous disease, inflammatory bowel disease,
				CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
				cells.	hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
449	HTLIF12	963	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt s lymphoma, non-Hodgkins lymphoma, Hodgkin's

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			tile man,	antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
		-		(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
			wa	Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
				may be used according to these assays are	include anemia, pancytopenia, leukopenia,
				publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
				ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
				used according to these assays include the	granulomatous disease, inflammatory bowel disease,
				CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
				cells.	hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
450	HTLF12	964	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,

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				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
	-			transcription through the GAS response	dysplasia. Preferred indications include autoimmune
	-			element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
		- 10		modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
	\ 1			(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
				may be used according to these assays are	include anemia, pancytopenia, leukopenia,
				publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
				ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
				used according to these assays include the	granulomatous disease, inflammatory bowel disease,
-	-			CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
				cells.	hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
451 HTLIF12		965	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STA1	pancreatic, esophageal, stomach, brain, liver and urinary

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			transcription factors and modulate gene	cancer. Other preferred indications include benign
			expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
			cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
			transcription through the GAS response	dysplasia. Preferred indications include autoimmune
			element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
			modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
			activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
			(including antibodies and agonists or	boosting a T cell-mediated immune response, and
			antagonists of the invention) include	suppressing a T cell-mediated immune response.
			assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
			66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
			Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
			Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
			85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
			Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
			Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
			4587 (1995), the contents of each of which	and/or an infectious disease as described below under
			are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
			entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
			may be used according to these assays are	include anemia, pancytopenia, leukopenia,
			publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
			ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
			used according to these assays include the	granulomatous disease, inflammatory bowel disease,
			CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
			culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
			cells.	hemophilia, hypercoagulation, diabetes mellitus,
				endocarditis, meningitis, Lyme Disease, and asthma and
				allergy.
452 HTNAM63 9	996	Activation of	Assays for the activation of transcription	Preferred indications include blood disorders (e.g., as
		transcription through	through the cAMP response element are	described below under "Immune Activity", "Blood-
		cAMP response	well-known in the art and may be used or	Related Disorders", and/or "Cardiovascular Disorders"),
		element in immune	routinely modified to assess the ability of	
		cells (such as T-cells).	polypeptides of the invention (including	below under "Infectious Disease"). Preferred
			antibodies and agonists or antagonists of	indications include autoimmune diseases (e.g., rheumatoid
			the invention) to increase cAMP and	arthritis, systemic lupus erythematosis, multiple sclerosis
			regulate CREB transcription factors, and	and/or as described below), immunodeficiencies (e.g., as
			modulate expression of genes involved in a	described below), boosting a 1 cell-mediated immune

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				wide variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune
				assays for transcription through the cAMP	response. Additional preferred indications include
				response element that may be used or	inflammation and inflammatory disorders. Highly
				routinely modified to test cAMP-response	preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Highly preferred
			:	agonists or antagonists of the invention)	indications include neoplasms and cancers, such as, for
				include assays disclosed in Berger et al.,	example, leukemia, lymphoma (e.g., T cell lymphoma,
				Gene 66:1-10 (1998); Cullen and Malm,	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				Methods in Enzymol 216:362-368 (1992);	disease), melanoma, and prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver and urinary
				85:6342-6346 (1988); Black et al., Virus	cancer. Other preferred indications include benign
				Genes 15(2):105-117 (1997); and	dysproliferative disorders and pre-neoplastic conditions,
				Belkowski et al., J Immunol 161(2):659-	such as, for example, hyperplasia, metaplasia, and/or
				665 (1998), the contents of each of which	dysplasia. Preferred indications include anemia,
				are herein incorporated by reference in its	pancytopenia, leukopenia, thrombocytopenia, acute
				entirety. T cells that may be used	lymphocytic anemia (ALL), plasmacytomas, multiple
				according to these assays are publicly	myeloma, arthritis, AIDS, granulomatous disease,
				available (e.g., through the ATCC).	inflammatory bowel disease, sepsis, neutropenia,
				Exemplary mouse T cells that may be used	neutrophilia, psoriasis, suppression of immune reactions to
				according to these assays include the	transplanted organs and tissues, hemophilia,
				CTLL cell line, which is a suspension	hypercoagulation, diabetes mellitus, endocarditis,
				culture of IL-2 dependent cytotoxic T	meningitis, Lyme Disease, and asthma and allergy.
				cells.	
453	HTNBK13	296	Regulation of viability	Assays for the regulation of viability and	A highly preferred indication is diabetes mellitus.
			and proliferation of	proliferation of cells in vitro are well-	An additional highly preferred indication is a complication
			pancreatic beta cells.	known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
				routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
				polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to regulate viability and	neuropathy, nerve disease and nerve damage (e.g., due to
				proliferation of pancreatic beta cells. For	diabetic neuropathy), blood vessel blockage, heart disease,
				example, the Cell Titer-Glo luminescent	stroke, impotence (e.g., due to diabetic neuropathy or
				cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion,
				viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
				quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
				signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,

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				active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
				used of fourmery modified to test regulation of viability and proliferation of	caldiovascular Disorders, section below), dysuplucinia, endocrine disorders (as described in the "Endocrine
				pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
				invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
				agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
				include assays disclosed in: Friedrichsen	diseases and disorders as described in the "Infectious
				BN, et al., Mol Endocrinol, 15(1):136-48	Diseases" section below, especially of the urinary tract and
				(2001); Huotari MA, et al., Endocrinology,	tunne
				139(4):1494-9 (1998); Hugl SR, et al., J	contracture). An additional highly preferred
				Biol Chem 1998 Jul 10;273(28):17771-9	indication is obesity and/or complications associated with
				(1998), the contents of each of which is	obesity. Additional highly preferred indications include
				herein incorporated by reference in its	weight loss or alternatively, weight gain. Aditional
				entirety. Pancreatic cells that may be used	highly preferred indications are complications associated
				according to these assays are publicly	with insulin resistance.
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
				cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
453	HTNBK13	296	Production of TNF	TNFa FMAT. Assays for	A highly preferred embodiment of the invention
	:		alpha by dendritic cells	immunomodulatory proteins produced by	includes a method for inhibiting (e.g., decreasing) TNF
				activated macrophages, T cells, fibroblasts,	alpha production. An alternative highly preferred
				smooth muscle, and other cell types that	embodiment of the invention includes a method for
				exert a wide variety of inflammatory and	stimulating (e.g., increasing) TNF alpha production.
				cytotoxic effects on a variety of cells are	Highly preferred indications include blood disorders (e.g.,
				well known in the art and may be used or	as described below under "Immune Activity", "Blood-
				routinely modified to assess the ability of	Related Disorders", and/or "Cardiovascular Disorders"),
				polypeptides of the invention (including	Highly preferred indications include autoimmune diseases
				antibodies and agonists or antagonists of	(e.g., rheumatoid arthritis, systemic lupus erythematosis,

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				the invention) to mediate	Crohn's disease multiple sclerosis and/or as described
				imminomodulation modulate	helow) imminodeficiencies (e o as described helow)
				inimidation of a state since The state of th	booting of all modisted immine account and
				inflammation and cytotoxicity. Exemplary	boosing a 1 cell-medialed infinding response, and
				assays that test for immunomodulatory	suppressing a 1 cell-mediated immune response.
				proteins evaluate the production of	Additional highly preferred indications include
				cytokines such as tumor necrosis factor	inflammation and inflammatory disorders, and treating
				alpha (TNFa), and the induction or	joint damage in patients with rheumatoid arthritis. An
				inhibition of an inflammatory or cytotoxic	additional highly preferred indication is sepsis. Highly
				response. Such assays that may be used or	preferred indications include neoplastic diseases (e.g.,
				routinely modified to test	leukemia, lymphoma, and/or as described below under
				immunomodulatory activity of	"Hyperproliferative Disorders"). Additionally, highly
				polypeptides of the invention (including	preferred indications include neoplasms and cancers, such
				antibodies and agonists or antagonists of	as, leukemia, lymphoma, melanoma, glioma (e.g.,
				the invention) include assays disclosed in	malignant glioma), solid tumors, and prostate, breast,
				Miraglia et al., J Biomolecular Screening	lung, colon, pancreatic, esophageal, stomach, brain, liver
				4:193-204(1999); Rowland et al.,	and urinary cancer. Other preferred indications include
				"Lymphocytes: a practical approach"	benign dysproliferative disorders and pre-neoplastic
				Chapter 6:138-160 (2000); Verhasselt et	conditions, such as, for example, hyperplasia, metaplasia,
				al., Eur J Immunol 28(11):3886-3890	and/or dysplasia. Preferred indications include anemia,
				(1198); Dahlen et al., J Immunol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				160(7):3585-3593 (1998); Verhasselt et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
	_			al., J Immunol 158:2919-2925 (1997); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				Nardelli et al., J Leukoc Biol 65:822-828	granulomatous disease, inflammatory bowel disease,
				(1999), the contents of each of which are	neutropenia, neutrophilia, psoriasis, suppression of
				herein incorporated by reference in its	immune reactions to transplanted organs and tissues,
				entirety. Human dendritic cells that may	hemophilia, hypercoagulation, diabetes mellitus,
				be used according to these assays may be	endocarditis, meningitis, Lyme Disease, cardiac
				isolated using techniques disclosed herein	reperfusion injury, and asthma and allergy. An
				or otherwise known in the art. Human	additional preferred indication is infection (e.g., an
				dendritic cells are antigen presenting cells	infectious disease as described below under "Infectious
				in suspension culture, which, when	Disease").
				activated by antigen and/or cytokines,	
				initiate and upregulate T cell proliferation	
				and functional activities.	
454	HTOAIS0 .	896		IFNgamma FMAT. IFNg plays a central	A highly preferred embodiment of the invention
			IFNgamma using a T	role in the immune system and is	includes a method for stimulating the production of IFNg.
			cells	considered to be a proinflammatory	An alternative highly preterred embodiment of the

_	cytokine. IFNg promotes I'H1 and	invention includes a method for inhibiting the production
	es	of IFNg. Highly preferred indications include blood
	ses	disorders (e.g., as described below under "Immune
	macrophage activation; and increases	Activity", "Blood-Related Disorders", and/or
	MHC expression. Assays for	"Cardiovascular Disorders"), and infection (e.g., viral
	immunomodulatory proteins produced by	infections, tuberculosis, infections associated with chronic
	T cells and NK cells that regulate a variety	granulomatosus disease and malignant osteoporosis,
	of inflammatory activities and inhibit TH2	and/or as described below under "Infectious Disease").
	helper cell functions are well known in the	Highly preferred indications include autoimmune disease
	art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
	to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
	invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
	agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
	mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
	inflammatory activities, modulate TH2	indications include inflammation and inflammatory
	helper cell function, and/or mediate	disorders. Additional preferred indications include
	humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
<u> </u>	Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
	immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
	production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
	gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
	cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
	routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
	immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
	polypeptides of the invention (including	include benign dysproliferative disorders and pre-
	antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
	the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
	in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
	Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
	al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
	Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
	J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
	Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
	(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
	15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
	(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
	of each of which are herein incorporated	

				by reference in its entirety. Human T cells	
				that may be used according to these assays	
				may be isolated using techniques disclosed	
				United T colleges animony burner	
				numan 1 cents are primary numan	
				lymphocytes that mature in the thymus and	
				express a T Cell receptor and CD3, CD4,	
				or CD8. These cells mediate numoral or	
				cell-mediated immunity and may be	
				preactivated to enhance responsiveness to	
				immunomodulatory factors.	
455	HTOAM11	696	Activation of	Assays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
			transcription through	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
			AP1 response element	known in the art and may be used or	blood disorders (e.g., as described below under "Immune
			in immune cells (such	routinely modified to assess the ability of	Activity", "Cardiovascular Disorders", and/or "Blood-
			as T-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious
				antibodies and agonists or antagonists of	disease as described below under "Infectious Disease").
				the invention) to modulate growth and	Highly preferred indications include autoimmune diseases
				other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				transcription through the AP1 response	multiple sclerosis and/or as described below) and
				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under
				assays disclosed in Berger et al., Gene	"Hyperproliferative Disorders"). Highly preferred
				66:1-10 (1988); Cullen and Malm,	indications include neoplasms and cancers, such as,
				Methods in Enzymol 216:362-368 (1992);	leukemia, lymphoma, prostate, breast, lung, colon,
				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver, and urinary
				85:6342-6346 (1988); Rellahan et al., J	cancer. Other preferred indications include benign
		-		Biol Chem 272(49):30806-30811 (1997);	dysproliferative disorders and pre-neoplastic conditions,
				Chang et al., Mol Cell Biol 18(9):4986-	such as, for example, hyperplasia, metaplasia, and/or
				4993 (1998); and Fraser et al., Eur J	dysplasia. Preferred indications include arthritis,
				Immunol 29(3):838-844 (1999), the	asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,
				contents of each of which are herein	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety. T	anemia (ALL), plasmacytomas, multiple myeloma,
				cells that may be used according to these	Burkitt's lymphoma, granulomatous disease, inflammatory

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			assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line	bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
455 HTOAMII	696	Activation of transcription through cAMP response element in immune cells (such as T-cells).	Assays for the activation of transcription through the cAMP response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to increase cAMP and regulate CREB transcription factors, and modulate expression of genes involved in a wide variety of cell functions. Exemplary assays for transcription through the cAMP response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Genes 15(2):105-117 (1997); and Belkowski et al., J Immunol 161(2):659-665 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the	Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders", and infectious disease as described below under "Infectious Disease"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional preferred indications include inflammatory disorders. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, ALDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia,
			Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is a suspension	neutrophilia, psoriasis, suppression of immune reac transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,

				culture of IL-2 dependent cytotoxic T cells.	meningitis, Lyme Disease, and asthma and allergy.
455	HTOAM11	696	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases
			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	onal
				entirety. Exemplary mouse T cells that	is idiopathic pulmonary fibrosis. Preferred indications
				may be used according to these assays are	include anemia, pancytopenia, leukopenia,
				publicly available (e.g., through the	thrombocytopenia, acute lymphocytic anemia (ALL),
				ATCC). Exemplary T cells that may be	plasmacytomas, multiple myeloma, arthritis, AIDS,
				used according to these assays include the	granulomatous disease, inflammatory bowel disease,
				CTLL cell line, which is a suspension	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				culture of IL-2 dependent cytotoxic T	immune reactions to transplanted organs and tissues,
				cells.	hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and

					allerov.
455	HTOAM11	696	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
	·			assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
				2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
				with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma,
					Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					neutrophilia, psoriasis, suppression of immune reactions to
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,

				meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication
				is infection (e.g., an infectious disease as described below under "Infectious Disease").
455 HTOAM11	696	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
		secretion from	are well-known in the art and may be used	An additional highly preferred indication is a complication
		pancreatic beta cells.	or routinely modified to assess the ability	associated with diabetes (e.g., diabetic retinopathy,
	-		of polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
		-	antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
			the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
			secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
			is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
			insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
			pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
			glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
			proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
		g, gamand	key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
			assays that may be used or routinely	stroke, and other diseases and disorders as described in the
			modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
			secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
			polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
			antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
			the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
			Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
			2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
			Endocrinology, 138(9):3735-40 (1997);	tunne
			Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
			(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
			Biomolecular Screening, 4:193-204	ications i
			(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
			herein incorporated by reference in its	highly preferred indications are complications associated
			entirety. Pancreatic cells that may be used	with insulin resistance.
			according to these assays are publicly	
			available (e.g., through the ATCC) and/or	
			may be routinely generated. Exemplary	
			pancreatic cells that may be used	
			according to these assays include rat INS-1	

			cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	
455 HTOAMII	696	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells. Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol 166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-2 production. Additional highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. An additional highly preferred indication includes infection (e.g., AIDS, and/or as described below under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, renal cell carcinoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for
			the ATCC). Exemplary human T cells that may be used according to these assays	example, melanoma (e.g., metastatic melanoma), renal cell carcinoma (e.g., metastatic renal cell carcinoma),

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				include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	leukemia, lymphoma (e.g., T cell lymphoma), and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred indication is infection (e.g., tuberculosis, infections associated with granulomatous disease, and osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). A highly preferred indication is AIDS. Additional highly preferred indications to transplanted organs and/or tissues, uveitis, psoriasis, and tropical spastic paraparesis. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arhritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
455 HTOAMII	4M11	696	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease

	art and may be used or routinely modified	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
-	to assess the ability of polypeptides of the	multiple sclerosis and/or as described below),
	invention (including antibodies and	immunodeficiency (e.g., as described below), boosting a T
	agonists or antagonists of the invention) to	cell-mediated immune response, and suppressing a T cell-
	mediate immunomodulation, regulate	mediated immune response. Additional highly preferred
	inflammatory activities, modulate TH2	indications include inflammation and inflammatory
	helper cell function, and/or mediate	disorders. Additional preferred indications include
	humoral or cell-mediated immunity.	idiopathic pulmonary fibrosis. Highly preferred
	Exemplary assays that test for	indications include neoplastic diseases (e.g., leukemia,
	immunomodulatory proteins evaluate the	lymphoma, melanoma, and/or as described below under
	production of cytokines, such as Interferon	"Hyperproliferative Disorders"). Highly preferred
	gamma (IFNg), and the activation of T	indications include neoplasms and cancers, such as, for
	cells. Such assays that may be used or	example, leukemia, lymphoma, melanoma, and prostate,
	routinely modified to test	breast, lung, colon, pancreatic, esophageal, stomach,
	immunomodulatory activity of	brain, liver and urinary cancer. Other preferred indications
	polypeptides of the invention (including	include benign dysproliferative disorders and pre-
	antibodies and agonists or antagonists of	neoplastic conditions, such as, for example, hyperplasia,
	the invention) include the assays disclosed	metaplasia, and/or dysplasia. Preferred indications
	in Miraglia et al., J Biomolecular	include anemia, pancytopenia, leukopenia,
	Screening 4:193-204 (1999); Rowland et	thrombocytopenia, Hodgkin's disease, acute lymphocytic
	al., "Lymphocytes: a practical approach"	anemia (ALL), plasmacytomas, multiple myeloma,
	Chapter 6:138-160 (2000); Gonzalez et al.,	Burkitt's lymphoma, arthritis, AIDS, granulomatous
	J Clin Lab Anal 8(5):225-233 (1995);	disease, inflammatory bowel disease, sepsis, neutropenia,
	Billiau et al., Ann NY Acad Sci 856:22-32	neutrophilia, psoriasis, suppression of immune reactions to
	(1998); Boehm et al., Annu Rev Immunol	transplanted organs and tissues, hemophilia,
	15:749-795 (1997), and Rheumatology	hypercoagulation, diabetes mellitus, endocarditis,
	(Oxford) 38(3):214-20 (1999), the contents	meningitis, Lyme Disease, asthma and allergy.
	of each of which are herein incorporated	
	by reference in its entirety. Human T cells	
	that may be used according to these assays	
	may be isolated using techniques disclosed	
	herein or otherwise known in the art.	
	Human T cells are primary human	
	lymphocytes that mature in the thymus and	
	express a T Cell receptor and CD3, CD4,	
	or CD8. These cells mediate humoral or	
	cell-mediated immunity and may be	

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				preactivated to enhance responsiveness to immunomodulatory factors.	
456	HTODH57	970	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkit's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
457	нторн83	971	Activation of	with cytotoxic activity. Assays for the activation of transcription	A preferred embodiment of the invention includes a
			serum response element	(SRE) are well-known in the art and may	method for infinition (e.g., reducing) the alpha production. An alternative preferred embodiment of the

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	in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
	as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
-	`	(including antibodies and agonists or	include blood disorders (e.g., as described below under
		antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
		the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
		the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
		growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
		transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
		used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
		activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
		invention (including antibodies and	immune response. Additional highly preferred indications
		agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
		include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
		Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
-		Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
		Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
		85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
		Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
		content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
		incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
		cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
		assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
		the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
		may be used according to these assays	
		include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred
		2 dependent suspension culture of T cells	indications include anemia, pancytopenia, leukopenia,
		with cytotoxic activity.	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			anemia (ALL), plasmacytomas, multiple myeloma,
		-	Burkitt's lymphoma, arthritis, AIDS, granulomatous
			disease, inflammatory bowel disease, neutropenia,
			neutrophilia, psoriasis, suppression of immune reactions to
			transplanted organs and tissues, hemophilia,
	244		hypercoagulation, diabetes mellitus, endocarditis,
			meningitis, Lyme Disease, cardiac reperfusion injury, and
			asthma and allergy. An additional preferred indication
			is infection (e.g., an infectious disease as described below
			under "Infectious Disease").

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Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders", and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Highly preferred indications also include boosting a B cell-
Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability
Production of ICAM-1	Production of IL-6
971	972
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457	458

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mediated immune response and alternatively suppressing a B cell-mediated immune response. Highly preferred indications include asthma and allergy. Highly preferred indications include asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for
of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-6, and the stimulation and upregulation of T cell proliferation and functional activities. Such assays that may be used or routinely modified to test immunomodulatory and differentiation activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the
	Activation of Natural Killer Cell ERK Signaling Pathway.
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				invention (including antibodies and	stimulating natural killer cell differentiation. An
				agonists or antagonists of the invention) to	alternative highly preferred embodiment of the invention
				promote or inhibit cell proliferation,	includes a method for inhibiting natural killer cell
				activation, and differentiation. Exemplary	differentiation. Highly preferred indications include
				assays for ERK kinase activity that may be	neoplastic diseases (e.g., as described below under
				used or routinely modified to test ERK	"Hyperproliferative Disorders"), blood disorders (e.g., as
				kinase-induced activity of polypeptides of	described below under "Immune Activity",
				the invention (including antibodies and	"Cardiovascular Disorders", and/or "Blood-Related
				agonists or antagonists of the invention)	Disorders"), immune disorders (e.g., as described below
				include the assays disclosed in Forrer et	under "Immune Activity") and infections (e.g., as
				al., Biol Chem 379(8-9):1101-1110	described below under "Infectious Disease"). Preferred
				(1998); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., as described
				64:29-48 (1999); Chang and Karin, Nature	below under "Immune Activity", "Blood-Related
				410(6824):37-40 (2001); and Cobb MH,	Disorders", and/or "Cardiovascular Disorders"). Highly
				Prog Biophys Mol Biol 71(3-4):479-500	preferred indications include autoimmune diseases (e.g.,
				(1999); the contents of each of which are	rheumatoid arthritis, systemic lupus erythematosis,
				herein incorporated by reference in its	multiple sclerosis and/or as described below) and
				entirety. Natural killer cells that may be	immunodeficiencies (e.g., as described below). Additional
				used according to these assays are publicly	highly preferred indications include inflammation and
				available (e.g., through the ATCC).	inflammatory disorders. Highly preferred indications
				Exemplary natural killer cells that may be	also include cancers such as, kidney, melanoma, prostate,
				used according to these assays include the	breast, lung, colon, pancreatic, esophageal, stomach,
				human natural killer cell lines (for	brain, liver, urinary cancer, lymphoma and leukemias.
				example, NK-YT cells which have	Other preferred indications include benign dysproliferative
				cytolytic and cytotoxic activity) or primary	disorders and pre-neoplastic conditions, such as, for
				NK cells.	example, hyperplasia, metaplasia, and/or dysplasia.
					Other highly preferred indications include, pancytopenia,
					leukopenia, leukemias, Hodgkin's disease, acute
					lymphocytic anemia (ALL), arthritis, asthma, AIDS,
					granulomatous disease, inflammatory bowel disease,
					sepsis, psoriasis, immune reactions to transplanted organs
					and tissues, endocarditis, meningitis, Lyme Disease, and
					allergies.
460	HTOH021	974	Activation of Adipocyte	Kinase assay. Kinase assays, for example	A highly preferred embodiment of the invention
			ERK Signaling	an Elk-1 kinase assay, for ERK signal	includes a method for stimulating adipocyte proliferation.
			Pathway	transduction that regulate cell proliferation	An alternative highly preferred embodiment of the
				or differentiation are well known in the art	invention includes a method for inhibiting adipocyte

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	and may be used or routinely modified to	aroliferation A highly preferred embodiment of the
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	invention (including antibodies and	differentiation. An alternative highly preferred
	agonists or antagonists of the invention) to	embodiment of the invention includes a method for
	promote or inhibit cell proliferation,	inhibiting adipocyte differentiation. A highly
	activation, and differentiation. Exemplary	preferred embodiment of the invention includes a method
	assays for ERK kinase activity that may be	for stimulating (e.g., increasing) adipocyte activation. An
	used or routinely modified to test ERK	alternative highly preferred embodiment of the invention
	kinase-induced activity of polypeptides of	includes a method for inhibiting the activation of (e.g.,
	the invention (including antibodies and	decreasing) and/or inactivating adipocytes. Highly
	agonists or antagonists of the invention)	preferred indications include endocrine disorders (e.g., as
	include the assays disclosed in Forrer et	described below under "Endocrine Disorders").
	al., Biol Chem 379(8-9):1101-1110	Highly preferred indications also include neoplastic
	(1998); Le Marchand-Brustel Y, Exp Clin	diseases (e.g., lipomas, liposarcomas, and/or as described
	Endocrinol Diabetes 107(2):126-132	below under "Hyperproliferative Disorders"). Preferred
	(1999); Kyriakis JM, Biochem Soc Symp	indications include blood disorders (e.g., hypertension,
	64:29-48 (1999); Chang and Karin, Nature	congestive heart failure, blood vessel blockage, heart
	410(6824):37-40 (2001); and Cobb MH,	disease, stroke, impotence and/or as described below
	Prog Biophys Mol Biol 71(3-4):479-500	under "Immune Activity", "Cardiovascular Disorders",
	(1999); the contents of each of which are	and/or "Blood-Related Disorders"), immune disorders
	herein incorporated by reference in its	(e.g., as described below under "Immune Activity"), neural
	entirety. Mouse adipocyte cells that may	disorders (e.g., as described below under "Neural Activity
	be used according to these assays are	and Neurological Diseases"), and infection (e.g., as
	publicly available (e.g., through the	described below under "Infectious Disease").
	ATCC). Exemplary mouse adipocyte cells	A highly preferred indication is diabetes mellitus. An
	that may be used according to these assays	additional highly preferred indication is a complication
	include 3T3-L1 cells. 3T3-L1 is an	associated with diabetes (e.g., diabetic retinopathy,
	adherent mouse preadipocyte cell line that	diabetic nephropathy, kidney disease (e.g., renal failure,
	is a continuous substrain of 3T3 fibroblast	nephropathy and/or other diseases and disorders as
	cells developed through clonal isolation	described in the "Renal Disorders" section below), diabetic
	and undergo a pre-adipocyte to adipose-	neuropathy, nerve disease and nerve damage (e.g., due to
	like conversion under appropriate	diabetic neuropathy), blood vessel blockage, heart disease,
	differentiation conditions known in the art.	stroke, impotence (e.g., due to diabetic neuropathy or
		blood vessel blockage), seizures, mental confusion,
		drowsiness, nonketotic hyperglycemic-hyperosmolar
		coma, cardiovascular disease (e.g., heart disease,
		atherosclerosis, microvascular disease, hypertension,

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HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		Coadiomiconior Disorders" section below) disclinidemia
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		Calulovasculai Disolucio sectioni eciow), ujsupiscuma,
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		endocrine disorders (as described in the "Endocrine
HTOHO21 974 Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway		Disorders" section below), neuropathy, vision impairment
HTOHO21 974 Activation of Skeletal Mucle Cell P13 Kinase Signalling Pathway		(e.g., diabetic retinopathy and blindness), ulcers and
HTOHO21 974 Activation of Skeletal Mucle Cell P13 Kinase Signalling Pathway		impaired wound healing, infection (e.g., infectious
HTOHO21 974 Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway		diseases and disorders as described in the "Infectious
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		Diseases" section below (particularly of the urinary tract
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		and skin). An additional highly preferred indication is
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		obesity and/or complications associated with obesity.
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		Additional highly preferred indications include weight loss
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		or alternatively, weight gain. Additional highly
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		preferred indications are complications associated with
HTOHO21 974 Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway		insulin resistance. Additional highly preferred
HTOHO21 974 Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway		indications are disorders of the musculoskeletal systems
HTOHO21 974 Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway		including myopathies, muscular dystrophy, and/or as
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		described herein. Additional highly preferred
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		indications include, hypertension, coronary artery disease,
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		dyslipidemia, gallstones, osteoarthritis, degenerative
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		arthritis, eating disorders, fibrosis, cachexia, and kidney
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		diseases or disorders. Preferred indications include
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		neoplasms and cancer, such as, lymphoma, leukemia and
HTOHO21 974 Activation of Skeletal Mucle Cell PI3 Kinase Signalling Pathway		breast, colon, and kidney cancer. Additional preferred
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		indications include melanoma, prostate, lung, pancreatic,
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		esophageal, stomach, brain, liver, and urinary cancer.
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		Highly preferred indications include lipomas and
HTOH021 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		liposarcomas. Other preferred indications include benign
HTOHO21 974 Activation of Skeletal Mucle Cell P13 Kinase Signalling Pathway		dysproliferative disorders and pre-neoplastic conditions,
HTOHO21 974 Activation of Skeletal Mucle Cell P13 Kinase Signalling Pathway		such as, for example, hyperplasia, metaplasia, and/or
HTOHO21 974 Activation of Skeletal Mucle Cell Pl3 Kinase Signalling Pathway		dysplasia.
		A highly preferred embodiment of the invention
		includes a method for increasing muscle cell survival An
metab	y signal transduction that regulate glucose	alternative highly preferred embodiment of the invention
1110a2	metabolism and cell survivial are well-	includes a method for decreasing muscle cell survival.
- NIOWI	known in the art and may be used or	A preferred embodiment of the invention includes a
routin	routinely modified to assess the ability of	method for stimulating muscle cell proliferation. In a
polypo	polypeptides of the invention (including	specific embodiment, skeletal muscle cell proliferation is

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antibodies and agonists or antagonists of	stimulated. An alternative highly preferred embodiment of
the invention) to promote or inhibit	the invention includes a method for inhibiting muscle cell
 glucose metabolism and cell survival.	proliferation. In a specific embodiment, skeletal muscle
Exemplary assays for PI3 kinase activity	cell proliferation is inhibited. A preferred embodiment
that may be used or routinely modified to	of the invention includes a method for stimulating muscle
test PI3 kinase-induced activity of	cell differentiation. In a specific embodiment, skeletal
polypeptides of the invention (including	muscle cell differentiation is stimulated. An alternative
antibodies and agonists or antagonists of	highly preferred embodiment of the invention includes a
the invention) include assays disclosed in	method for inhibiting muscle cell differentiation. In a
 Forrer et al., Biol Chem 379(8-9):1101-	specific embodiment, skeletal muscle cell differentiation is
1110 (1998); Nikoulina et al., Diabetes	inhibited. Highly preferred indications include disorders
49(2):263-271 (2000); and Schreyer et al.,	of the musculoskeletal system. Preferred indications
Diabetes 48(8):1662-1666 (1999), the	include neoplastic diseases (e.g., as described below under
contents of each of which are herein	"Hyperproliferative Disorders"), endocrine disorders (e.g.,
incorporated by reference in its entirety.	as described below under "Endocrine Disorders"), neural
Rat myoblast cells that may be used	disorders (e.g., as described below under "Neural Activity
according to these assays are publicly	and Neurological Diseases"), blood disorders (e.g., as
available (e.g., through the ATCC).	described below under "Immune Activity",
Exemplary rat myoblast cells that may be	"Cardiovascular Disorders", and/or "Blood-Related
used according to these assays include L6	Disorders"), immune disorders (e.g., as described below
cells. L6 is an adherent rat myoblast cell	, as
line, isolated from primary cultures of rat	¥
 thigh muscle, that fuses to form	highly preferred indication is diabetes mellitus.
multinucleated myotubes and striated	additional highly preferred indication is a complication
fibers after culture in differentiation media.	associated with diabetes (e.g., diabetic retinopathy,
	diabetic nephropathy, kidney disease (e.g., renal failure,
	nephropathy and/or other diseases and disorders as
	described in the "Renal Disorders" section below), diabetic
	neuropathy, nerve disease and nerve damage (e.g, due to
	diabetic neuropathy), blood vessel blockage, heart disease,
	stroke, impotence (e.g., due to diabetic neuropathy or
	blood vessel blockage), seizures, mental confusion,
	drowsiness, nonketotic hyperglycemic-hyperosmolar
	coma, cardiovascular disease (e.g., heart disease,
	atherosclerosis, microvascular disease, hypertension,
	stroke, and other diseases and disorders as described in the
	"Cardiovascular Disorders" section below), dyslipidemia,

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		chemotaxis, and modulate T cell differentiation. Exemplary assays that test for immunomodulatory proteins evaluate the production of chemokines, such as macrophage inflammatory protein 1 alpha (MIP-1a), and the activation of monocytes/macrophages and T cells. Such assays that may be used or routinely modified to test immunomodulatory and chemotaxis activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); Drakes et al., Transp Immunol 8(1):17-29 (2000); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma, and allergy. Preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysplasia. dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
HТОЛ.95 976	Upregulation of CD71 and activation of T cells	CD71 FMAT. CD71 is the transferrin receptor. Transferrin is a major iron carrying protein that is essential for cell proliferation. CD71 is expressed predominantly on cells that are actively	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. Preferred indications include blood disorders (e.g., as

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A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious	Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. Additional highly preferred indications include infection. Preferred	indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia,	pancytopenia, reukopenia, unombocytopenia, rougkin signisease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
CD71 FMAT. CD71 is the transferrin receptor. Transferrin is a major iron carrying protein that is essential for cell proliferation. CD71 is expressed predominantly on cells that are actively proliferating. Assays for immunomodulatory proteins expressed on activated T cells. B cells, and most	proliferating cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the	upregulation of cell surface markers, such as CD71, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a	practical approach Chapter 0:138-100 (2000); and Afetra et al., Ann Rheum Dis 52(6):457-460 (1993), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human I with the thymus and I ymphocytes that mature in the thymus and
Upregulation of CD71 and activation of T cells			
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			express a T Cell receptor and CD3, CD4.	
			or CD8. These cells mediate humoral or	
			cell-mediated immunity and may be	
			preactivated to enhance responsiveness to	
			immunomodulatory factors.	
464 HTPDU17	8/6 /	Production of IL-4	L-4 FMAT. Assays for	A highly preferred embodiment of the invention
			immunomodulatory proteins secreted by	includes a method for stimulating (e.g., increasing) IL-4
			TH2 cells that stimulate B cells, T cells,	production. An alternative highly preferred embodiment of
			macrophages and mast cells and promote	ફ
			polarization of CD4+ cells into TH2 cells	reducing) IL-4 production. A highly preferred
			are well known in the art and may be used	indication includes asthma. A highly preferred
			or routinely modified to assess the ability	indication includes allergy. A highly preferred
			of polypeptides of the invention (including	indication includes rhinitis. Additional highly preferred
			antibodies and agonists or antagonists of	indications include inflammation and inflammatory
			the invention) to mediate	disorders. Highly preferred indications include
			immunomodulation, stimulate immune	neoplastic diseases (e.g., leukemia, lymphoma,
			cells, modulate immune cell polarization,	melanoma, and/or as described below under
			and/or mediate humoral or cell-mediated	"Hyperproliferative Disorders"). Preferred indications
			immunity. Exemplary assays that test for	include neoplasms and cancers, such as, for example,
			immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and prostate, breast,
			production of cytokines, such as IL-4, and	lung, colon, pancreatic, esophageal, stomach, brain, liver
			the stimulation of immune cells, such as B	and urinary cancer. Other preferred indications include
,			cells, T cells, macrophages and mast cells.	benign dysproliferative disorders and pre-neoplastic
-			Such assays that may be used or routinely	conditions, such as, for example, hyperplasia, metaplasia,
			modified to test immunomodulatory	and/or dysplasia. Preferred indications include blood
			activity of polypeptides of the invention	disorders (e.g., as described below under "Immune
			(including antibodies and agonists or	Activity", "Blood-Related Disorders", and/or
***			antagonists of the invention) include the	"Cardiovascular Disorders"). Preferred indications include
			assays disclosed in Miraglia et al., J	autoimmune diseases (e.g., rheumatoid arthritis, systemic
			Biomolecular Screening 4:193-204 (1999);	lupus erythematosis, multiple sclerosis and/or as described
			Rowland et al., "Lymphocytes: a practical	below) and immunodeficiencies (e.g., as described below).
-			approach" Chapter 6:138-160 (2000);	Preferred indications include anemia, pancytopenia,
			Gonzalez et al., J Clin Lab Anal 8(5):277-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
			283 (1194); Yssel et al., Res Immunol	lymphocytic anemia (ALL), plasmacytomas, multiple
			144(8):610-616 (1993); Bagley et al., Nat	myeloma, Burkitt's lymphoma, arthritis, AIDS,
			Immunol 1(3):257-261 (2000); and van der	granulomatous disease, inflammatory bowel disease,
			Graaff et al., Rheumatology (Oxford)	sepsis, neutropenia, neutrophilia, psoriasis, suppression of

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	Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cellmediated immunity and may be preactivated to enhance responsiveness to	infectious disease as described below under "Infectious Disease").
Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the serum response of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors,
	m response element mune cells (such cells).	uch (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these

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stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for increasing muscle cell survival An alternative highly preferred embodiment of the invention includes a method for decreasing muscle cell survival. A preferred embodiment of the invention includes a method for stimulating muscle cell proliferation. In a specific embodiment, skeletal muscle cell proliferation is stimulated. An alternative highly preferred embodiment of the invention includes a method for inhibiting muscle cell proliferation. In a specific embodiment, skeletal muscle cell differentiation is inhibited. A preferred embodiment of the invention includes a method for stimulating muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation. In a specific embodiment of the invention includes a method for inhibiting muscle cell differentiation. In a specific embodiment, skeletal muscle cell differentiation is inhibited. Highly preferred indications include disorders of the musculoskeletal system. Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), endocrine disorders (e.g.,
stomach, b indications pre-neoplasia hyperplasia indications thrombocyt anemia (Al Burkitt's ly disease, inf neutrophili- transplante- hypercoagu meningitis, asthma and is infection under "Infe	A highly includes a palternative includes a palternative includes at A preferre method for specific en stimulated, the inventive proliferation of the invecell different muscle cell highly preferation of the method for specific en inhibited. of the muss include near "Hyperpro
assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	Kinase assay. Kinase assays, for example an GSK-3 kinase assay, for PI3 kinase signal transduction that regulate glucose metabolism and cell survivial are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit glucose metabolism and cell survival. Exemplary assays for PI3 kinase activity that may be used or routinely modified to test PI3 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Nikoulina et al., Diabetes 49(2):263-271 (2000); and Schreyer et al., Diabetes 48(8):1662-1666 (1999), the contents of each of which are herein
	Activation of Skeletal Mucle Cell P13 Kinase Signalling Pathway
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incorporated by reference in its entirety. Rat myoblast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary rat myoblast cells that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuses to form multinucleated myotubes and striated fibers after culture in differentiation media.	as described below under "Endocrine Disorders"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Infectious Disease"). An highly preferred indication is diabetes mellitus. An additional highly preferred indication is diabetec retinopathy, diabetes (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dvslipidemia,
	cadocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, infections (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications are complications associated with insulin resistance. Additional highly preferred indications are disorders of the musculoskeletal system indications are disorders of the musculoskeletal system

described herein. Additional highly preferred indications include: myopathy, atrophy, congestive heart failure, cachexia, myxomas, fibromas, congenital cardiovascular abnormalities, heart disease, cardiac arrest, heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.	t and may be used An additional highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication assess the ability diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular diseases (e.g., heart disease, atherosclerosis, microalscreases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's indication is obesity andor complication associated with
	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of
	Stimulation of insulin secretion from pancreatic beta cells.
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weig weigh highl	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious
Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Satin LS, et al., Endocrinology,
	Stimulation of Calcium Flux in pancreatic beta cells.
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Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing)
136(10):4589-601 (1995);Mogami H, et al., Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al., Cell Calcium 1989 Nov-Dec;10(8):535-41 (1989), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase protease-mediated apoptosis. Induction of apoptosis in endothelial cells supporting the vasculature of tumors is associated with tumor regression due to loss of tumor blood supply. Exemplary assays for caspase apoptosis that may be used or routinely
	Endothelial Cell Apoptosis
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modified to test capase apoptosis activity	apoptosis of endothelial cells. A highly preferred
of polypeptides of the invention (including	nclude
antibodies and agonists or antagonists of	stimulating angiogenisis. An alternative highly preferred
the invention) include the assays disclosed	embodiment of the invention includes a method for
in Lee et al., FEBS Lett 485(2-3): 122-126	inhibiting angiogenesis. A highly preferred
(2000); Nor et al., J Vasc Res 37(3): 209-	embodiment of the invention includes a method for
218 (2000); and Karsan and Harlan, J	reducing cardiac hypertrophy. An alternative highly
Atheroscler Thromb 3(2): 75-80 (1996);	preferred embodiment of the invention includes a method
the contents of each of which are herein	for inducing cardiac hypertrophy. Highly preferred
incorporated by reference in its entirety.	indications include neoplastic diseases (e.g., as described
Endothelial cells that may be used	below under "Hyperproliferative Disorders"), and
according to these assays are publicly	disorders of the cardiovascular system (e.g., heart disease,
available (e.g., through commercial	congestive heart failure, hypertension, aortic stenosis,
sources). Exemplary endothelial cells that	cardiomyopathy, valvular regurgitation, left ventricular
may be used according to these assays	dysfunction, atherosclerosis and atherosclerotic vascular
include bovine aortic endothelial cells	disease, diabetic nephropathy, intracardiac shunt, cardiac
(bAEC), which are an example of	hypertrophy, myocardial infarction, chronic hemodynamic
endothelial cells which line blood vessels	overload, and/or as described below under
and are involved in functions that include,	"Cardiovascular Disorders"). Highly preferred indications
but are not limited to, angiogenesis,	include cardiovascular, endothelial and/or angiogenic
vascular permeability, vascular tone, and	disorders (e.g., systemic disorders that affect vessels such
immune cell extravasation.	as diabetes mellitus, as well as diseases of the vessels
	themselves, such as of the arteries, capillaries, veins and/or
	lymphatics). Highly preferred are indications that
	stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis
	and/or cardiovascularization. Highly preferred
	indications include antiangiogenic activity to treat solid
	tumors, leukemias, and Kaposi's sarcoma, and retinal
	disorders. Highly preferred indications include neoplasms
	and cancer, such as, Kaposi's sarcoma, hemangioma
	(capillary and cavernous), glomus tumors, telangiectasia,
	bacillary angiomatosis, hemangioendothelioma,
	angiosarcoma, haemangiopericytoma, lymphangioma,
	lymphangiosarcoma. Highly preferred indications also
	include cancers such as, prostate, breast, lung, colon,
	pancreatic, esophageal, stomach, brain, liver, and urinary

					cancer. Preferred indications include benign
					dysproliferative disorders and pre-neoplastic conditions,
					such as, for example, hyperplasia, metaplasia, and/or
					dysplasia. Highly preferred indications also include
					arterial disease, such as, atherosclerosis, hypertension,
					coronary artery disease, inflammatory vasculitides,
					Reynaud's disease and Reynaud's phenomenom,
					aneurysms, restenosis; venous and lymphatic disorders
					such as thrombophlebitis, lymphangitis, and lymphedema;
					and other vascular disorders such as peripheral vascular
					disease, and cancer. Highly preferred indications also
					include trauma such as wounds, burns, and injured tissue
					(e.g., vascular injury such as, injury resulting from balloon
					angioplasty, and atheroschlerotic lesions), implant
					fixation, scarring, ischemia reperfusion injury, rheumatoid
					arthritis, cerebrovascular disease, renal diseases such as
					acute renal failure, and osteoporosis. Additional highly
					preferred indications include stroke, graft rejection,
					diabetic or other retinopathies, thrombotic and coagulative
					disorders, vascularitis, lymph angiogenesis, sexual
					disorders, age-related macular degeneration, and treatment
					/prevention of endometriosis and related conditions.
					Additional highly preferred indications include fibromas,
					heart disease, cardiac arrest, heart valve disease, and
					vascular disease. Preferred indications include blood
					disorders (e.g., as described below under "Immune
					Activity", "Blood-Related Disorders", and/or
					"Cardiovascular Disorders"). Preferred indications include
					autoimmune diseases (e.g., rheumatoid arthritis, systemic
					lupus erythematosis, multiple sclerosis and/or as described
					below) and immunodeficiencies (e.g., as described below).
					Additional preferred indications include inflammation and
					inflammatory disorders (such as acute and chronic
					inflammatory diseases, e.g., inflammatory bowel disease
					and Crohn's disease), and pain management.
469	HTWEH94	883	Stimulation of insulin	Assays for measuring secretion of insulin	A highly preferred indication is diabetes mellitus.
			secretion from	are well-known in the art and may be used	An additional nigniy preferred indication is a complication

	11	and it is a second of the second the shillifter	accompany with disheter (e.g. dishetic retinonathy
	pancicatic octa cens.	of polymentides of the invention (including	dishetic nenhronathy kidney disease (e.g. renal failure
		antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
		the invention) to stimulate insulin	described in the "Renal Disorders" section below), diabetic
	•	secretion. For example, insulin secretion	neuropathy, nerve disease and nerve damage (e.g., due to
		is measured by FMAT using anti-rat	diabetic neuropathy), blood vessel blockage, heart disease,
		insulin antibodies. Insulin secretion from	stroke, impotence (e.g., due to diabetic neuropathy or
		pancreatic beta cells is upregulated by	blood vessel blockage), seizures, mental confusion,
		glucose and also by certain	drowsiness, nonketotic hyperglycemic-hyperosmolar
		proteins/peptides, and disregulation is a	coma, cardiovascular disease (e.g., heart disease,
		key component in diabetes. Exemplary	atherosclerosis, microvascular disease, hypertension,
	-	assays that may be used or routinely	stroke, and other diseases and disorders as described in the
		modified to test for stimulation of insulin	"Cardiovascular Disorders" section below), dyslipidemia,
		secretion (from pancreatic cells) by	endocrine disorders (as described in the "Endocrine
		polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
		antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
		the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
		Ahren, B., et al., Am J Physiol, 277(4 Pt	diseases and disorders as described in the "Infectious
		2):R959-66 (1999); Li, M., et al.,	Diseases" section below, especially of the urinary tract and
		Endocrinology, 138(9):3735-40 (1997);	skin), carpal tunnel syndrome and Dupuytren's
		Kim, K.H., et al., FEBS Lett, 377(2):237-9	contracture). An additional highly preferred
	-	(1995); and, Miraglia S et. al., Journal of	indication is obesity and/or complications associated with
		Biomolecular Screening, 4:193-204	obesity. Additional highly preferred indications include
		(1999), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
		herein incorporated by reference in its	highly preferred indications are complications associated
		entirety. Pancreatic cells that may be used	with insulin resistance.
		according to these assays are publicly	
		available (e.g., through the ATCC) and/or	
		may be routinely generated. Exemplary	-
		pancreatic cells that may be used	
		according to these assays include rat INS-1	
-		cells. INS-1 cells are a semi-adherent cell	
		line established from cells isolated from an	
		X-ray induced rat transplantable	
		insulinoma. These cells retain	
		characteristics typical of native pancreatic	
		beta cells including glucose inducible	

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			insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	
470 HTXBD09	884	Activation of transcription through NFKB response element in epithelial cells (such as HELA cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of epithhelial genes. Exemplary assays for transcription through the NFKB response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Kaltschmidt B, et al., Oncogene, 18(21):3213-3225 (1999); Beetz A, et al., Int J Radiat Biol, 76(11):1443-1453 (2000); Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Valle Blazquez et al., Immunology 90(3):455-460 (1997); Aramburau et al., 1 Exp Med 82(3):801-810 (1995); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Epithelial cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Wound Healing, and Inflamation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include include inflammation and inflammatory disorders.
			used according to these assays include the HELA cell line.	
471 HTXDB22	985	Activation of	Assays for the activation of transcription	Highly preferred indications include neoplastic diseases

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			transcription through	through the Gamma Interferon Activation	(e.g., leukemia, lymphoma, and/or as described below
			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or routinely modified to assess the ability of	indications include neoplasms and cancers, such as, for example lenkemia lymphoma (e.g., T.cell lymphoma
			43 1-Cells).	nolypentides of the invention (including	Example, teunchina, ijimphonia (e.g., 1 cen ijimphonia, Burkiti's lymphoma, hodokin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
				transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
•••				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary human T cells, such	is idiopathic pulmonary fibrosis. Preferred indications
				as the SUPT cell line, that may be used	include anemia, pancytopenia, leukopenia,
				according to these assays are publicly	thrombocytopenia, acute lymphocytic anemia (ALL),
				available (e.g., through the ATCC).	plasmacytomas, multiple myeloma, arthritis, AIDS,
-					granulomatous disease, inflammatory bowel disease,
					sepsis, neutropenia, neutrophilia, psoriasis, suppression of
					immune reactions to transplanted organs and tissues,
-					hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
+	1				allergy.
472 HTXDC38		986	Activation of transcription through	Assays for the activation of transcription through the Gamma Interferon Activation	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below

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			GAS response element	Site (GAS) response element are well-	under "Hyperproliferative Disorders"). Highly preferred
			in immune cells (such	known in the art and may be used or	indications include neoplasms and cancers, such as, for
			as T-cells).	routinely modified to assess the ability of	example, leukemia, lymphoma (e.g., T cell lymphoma,
				polypeptides of the invention (including	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				antibodies and agonists or antagonists of	disease), melanoma, and prostate, breast, lung, colon,
				the invention) to regulate STAT	pancreatic, esophageal, stomach, brain, liver and urinary
			,	transcription factors and modulate gene	cancer. Other preferred indications include benign
				expression involved in a wide variety of	dysproliferative disorders and pre-neoplastic conditions,
				cell functions. Exemplary assays for	such as, for example, hyperplasia, metaplasia, and/or
				transcription through the GAS response	dysplasia. Preferred indications include autoimmune
				element that may be used or routinely	diseases (e.g., rheumatoid arthritis, systemic lupus
				modified to test GAS-response element	erythematosis, multiple sclerosis and/or as described
				activity of polypeptides of the invention	below), immunodeficiencies (e.g., as described below),
				(including antibodies and agonists or	boosting a T cell-mediated immune response, and
				antagonists of the invention) include	suppressing a T cell-mediated immune response.
				assays disclosed in Berger et al., Gene	Additional preferred indications include inflammation and
				66:1-10 (1998); Cullen and Malm,	inflammatory disorders. Highly preferred indications
				Methods in Enzymol 216:362-368 (1992);	include blood disorders (e.g., as described below under
				Henthorn et al., Proc Natl Acad Sci USA	"Immune Activity", "Blood-Related Disorders", and/or
				85:6342-6346 (1988); Matikainen et al.,	"Cardiovascular Disorders"), and infection (e.g., viral
				Blood 93(6):1980-1991 (1999); and	infections, tuberculosis, infections associated with chronic
				Henttinen et al., J Immunol 155(10):4582-	granulomatosus disease and malignant osteoporosis,
				4587 (1995), the contents of each of which	and/or an infectious disease as described below under
				are herein incorporated by reference in its	"Infectious Disease"). An additional preferred indication
				entirety. Exemplary human T cells, such	is idiopathic pulmonary fibrosis. Preferred indications
_				as the SUPT cell line, that may be used	include anemia, pancytopenia, leukopenia,
				according to these assays are publicly	thrombocytopenia, acute lymphocytic anemia (ALL),
				available (e.g., through the ATCC).	plasmacytomas, multiple myeloma, arthritis, AIDS,
					granulomatous disease, inflammatory bowel disease,
					sepsis, neutropenia, neutrophilia, psoriasis, suppression of
					immune reactions to transplanted organs and tissues,
					hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and
					allergy.
473	HTXDC77	186	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SINE) are well-kilowii iii tile art alid iliay	production. An alternative inginy preferred emoodiment of

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	in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
	as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
		(including antibodies and agonists or	include blood disorders (e.g., as described below under
		antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
		serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
		expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
		and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
		related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
		Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
		the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
		modified to test SRE activity of the	immune response. Additional highly preferred indications
		polypeptides of the invention (including	include inflammation and inflammatory disorders, and
		antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
		the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
		Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
		and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
		368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
		Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
		Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
		3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
		12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
		of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
		reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
		be used according to these assays are	pre-neoplastic conditions, such as, for example,
		publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
		ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,
		used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic
	•	NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,
		killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous
		activity.	disease, inflammatory bowel disease, neutropenia,
			neutrophilia, psoriasis, suppression of immune reactions to
			transplanted organs and tissues, hemophilia,
			hypercoagulation, diabetes mellitus, endocarditis,
			meningitis, Lyme Disease, cardiac reperfusion injury, and
			asthma and allergy. An additional preferred indication
			is infection (e.g., an infectious disease as described below
			under "Infectious Disease").

A highly preferred embodiment of the invention includes a method for activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention includes a method for activation B cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating B cells. A highly preferred embodiment of the invention includes a method for activating NK cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting activation of and/or inactivation NK cells. Highly preferred indications include inflammation and inflammatory disorders (e.g., as described below under "Immune Activity"). Preferred indications include blood	disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response and alternatively suppressing a T cell-mediated immune response, and boosting a B cell-mediated immune response. An additional highly preferred immune response. An additional highly preferred indication includes infection (e.g., as described below under "Infectious Disease"). Preferred indications also include aremia paracutonenia lanconical	thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,
CD69 FMAT. CD69 is an activation marker that is expressed on activated T cells, B cells, and NK cells. CD69 is not expressed on resting T cells, B cells, or NK cells. CD69 has been found to be associated with inflammation. Assays for immunomodulatory proteins expressed in T cells, B cells, and leukocytes are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cellmediated immunity. Exemplary assays that test for immunomodulatory proteins	evaluate the upregulation of cell surface markers, such as CD69, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Ferenczi et al., J Autoimmun 14(1):63-78	(1997); Taylor-Fishwick and Siegel, Eur J Immunol 25(12):3215-3221 (1995); and Afetra et al., Ann Rheum Dis 52(6):457-460 (1993), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated
Upregulation of CD69 and activation of T cells		
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Human T cells inflammatory disorders, asthma, and allergies. Preferred indications also include neoplastic diseases (e.g., sxpress a T Cell eukemia, lymphoma, and/or as described below under r CD8. These "Hyperproliferative Disorders"). Preferred indications include neoplasms, such as, for example, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	f f f W.,
using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	Kinase assays, for example kinase assays for members of the MAP kinase family (including p38, JAK, and ERK) are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, differentiation, and/or cytokine production in immune cells such as T-cells. Exemplary assays for MAP kinase family members that may be used or routinely modified to test polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Rincon M., Curr Opin Immunol; 13(3):339-345 (2001); Wang LH, et al., J Immunol, 162(7):3897-3904 (1999); Sakamoto H, et al., J Biol Chem, 275(46):35857-35862 (2000), the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells (for example, T-cells) that may be used according to these assays include the mouse CTLL cell line.
	Proliferation, and/or cytokine production in immune cells (such as T-cells).
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Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkit's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dyspolasia. Preferred indications include benign auch as, for axample, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoi arthritis, systemic lupus erythematosis, multiple solerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response, and inflammatory disorders. Elighly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease as described below under "Infectious Disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease,"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indication is idiopathic pulmonary fibrosis. Preferred indication is idiopathic pulmonary theorogulation, disease, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, mentinetics. Lymp Basase, and asthma and asthma and	allergy. Preferred embodiments of the invention include using
Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the SUPT cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).	Kinase assays, for example kinase assays
Activation of transcription through GAS response element in immune cells (such as T-cells).	Proliferation,
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polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of inflammation, infection, allergy, asthma, autoimmunity, and cancer.		A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease,
for members of the MAP kinase family (including p38, JAK, and ERK) are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of	the invention) to promote or inhibit cell proliferation, differentiation, and/or cytokine production in immune cells such as T-cells. Exemplary assays for MAP kinase family members that may be used or routinely modified to test polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in: Rincon M., Curr Opin Immunol; 13(3):339-345 (2001); Wang LH, et al., J Immunol, 162(7):3897-3904 (1999); Sakamoto H, et al., J Biol Chem, 275(46):35857-35862 (2000), the contents of each of which are herein incorporated by reference in its entirety. Exemplary immune cells (for example, T-cells) that may be used according to these assays include the mouse CTLL cell line.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to
differentiation, and/or cytokine production in immune cells (such as T-cells).		Stimulation of Calcium Flux in pancreatic beta cells.
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			activation of calcium responsive signaling pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Satin LS, et al., Endocrinology, 136(7):2960-6 (1995); Richardson SB, et al., Biochem J, 288 (Pt 3):847-51 (1992); and, Meats, JE, et al., Cell Calcium 1989 Nov-Dec;10(8):535-41 (1989), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cells transformed with SV40. These cells express glucagon, somatostatin, and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Defer Lord and Arbardf, Biochem 1 210.	atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia, endocrine disorders (as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious Diseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications associated with insulin resistance.
			Kets: Lord and Asnerott. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	
478 HTXJY08	992	Activation of transcription through NFAT response element in immune	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include
		cells (such as natural	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic

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antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays are publicly available (e.g., through the Serum Response Element SRE) are well-known in the art and may cells (such ability of polypeptides of the invention ability of polypeptides of the invention				killer cells).	nolyneptides of the invention (including	lupus ervthematosis, multiple sclerosis and/or as described
the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antipodies and agonists or anagonists of anagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:326-368 (1992); Henthorn et al., Proc Nall Acad Sci USA SS:6342-6346 (1998); Aramburu et al., J Exp Med 182(3):801-810 (1995); and Yeseen et al., If Biol Chem 268(19):14285- 14293 (1993), the contents of each of which are herein incorporated by reference in its entirely. NR cells that may be used according to these assays are publicly activity. HITXIYO8 Activation of Assays for the activation of transcription transcription through Assays for the activation of transcription transcription through the Serum Response Element serum response element (SRE) are well-known in the art and may in immune cells (such as natural killer cells). ability of polypeptides of the invention					antibodies and agonists or antagonists of	below), immunodeficiencies (e.g., as described below),
ranscription factors and modulate cxpression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assay disclosed in Berger et al., Gene 66.1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); available te al., in its entirety. NK cells that may be used according to these assays are publicity available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays are publicity available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. Assays for the activation of transcription transcription through transcription through through the Serum Response Element serum response element serum response element be used or routinely modified to assess the as natural killer cells). ability of polypeptides of the invention					the invention) to regulate NFAT	boosting a T cell-mediated immune response, and
expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 21 (6:362-368 (1992); Henthom et al., Pro: Nall Acad Sci USA 85:6342-6346 (1988); Arambur et al., DE EXP Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1995); De Boer et al., De Contents of each of which are herein incorporated by reference in its entirety. Nicells that may be used according to these assays are publicity available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays are publicity available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. HTXJY08 Activation of Assays for the activation of transcription through the Archive in a human natural serium response element serium esponse element serium response ele					transcription factors and modulate	suppressing a T cell-mediated immune response.
immunomodulatory functions. Exemplary assays for transcription through the NFAT response element activity of polypeptides of the invention (including antibodies and agonists or anagomists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988), Arambur et al., J Brophom et al., Prox Natl Acad Sci USA 85:6342-6346 (1988), Arambur et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); and Yeseen et al., J Biol Chem 268(19):1428-14286 (1993); the contents of each of which are herein incorporated by reference in its entirety. Natl anay be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. Activation of Assays for the activation of transcription transcription through the Serum Response Element s					expression of genes involved in	Additional highly preferred indications include
assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):121-1236 (1995); Praser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. Activation of Assays for the activation of transcription transcription through the Serum Response Element Serum response element (SRE) are well-known in the art and may in immune cells (such as natural killer cells) ability of polypeptides of the invention					immunomodulatory functions. Exemplary	inflammation and inflammatory disorders. An additional
response element that may be used or routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66.1-10 (1998); Culten and Malm, Methods in Enzymol 216:362-368 (1992); Henthom et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J. Exp Med 182(3):801-810 (1995); De Boer et al., Int Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur JI (10):1221-1236 (1999); Fraser et al., Eur JI (10):1221-1236 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell ine with cytolytic and cytotoxic activity. HTXJY08 992 Activation of Assays for the activation of transcription transcription through the Serum Response Element Serum response element (SRE) are well-known in the art and may in immune cells (such be used or routinely modified to assess the ability of polypeptides of the invention					assays for transcription through the NFAT	highly preferred indication is infection (e.g., an infectious
routinely modified to test NFAT-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthron et al., Pro Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1992), the contents of each of which are heretin incorporated by reference in its entirety. NR cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplay human NR cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplay human NR cells that may be used according to these assays include the NR-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. HTXJY08 992 Activation of Assays for the activation of transcription through through the Serum Response Element serum response element (SRE) are well-known in the art and may in immune cells (such a builty of polypeptides of the invention					response element that may be used or	disease as described below under "Infectious Disease").
element activity of polypeptides of the invention (including antibodies and agonits or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochen Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):83-8-84 (1999); and Yessen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. HTXJY08 992 Activation of Assays for the activation of transcription transcription through the Serum Response Element serum response element (SRE) are well-known in the art and may in immune cells (such ability of polypeptides of the invention					routinely modified to test NFAT-response	Preferred indications include neoplastic diseases (e.g.,
invention (including antibodies and agonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1922); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. HTXJY08 Activation of Assays for the activation of transcription transcription through the Serum Response Element serum response element (SRE) are well-known in the art and may in immune cells (such as natural killer cells). Ability of polypeptides of the invention					element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Y reseen et al., Int J Biol Chem 268(19):14285- 14293 (1993); the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. Assays for the activation of transcription transcription through the Serum Response Element serum response element in immune cells (such as natural killer cells). biologeness of the invention					invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285- 14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. HTXJY08 PACIVATION Assays for the activation of transcription transcription through the Serum Response Element serum response element (SRE) are well-known in the art and may in immune cells (such ability of polypeptides of the invention			***************************************		agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285- 14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. Assays for the activation of transcription transcription through the Serum Response Element serum response element in immune cells (such as natural killer cells). ability of polypeptides of the invention					include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., In1 Biochem Cell Biol 31(10):1221-1236 (1999); Praser et al., Eur J Immunol 29(3):838-844 (1999); and Yessen et al., J Biol Chem 268(19):14285-14293 (1993); the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. HTXJY08 Activation of through the Serum Response Element serum response element (SRE) are well-known in the art and may in immune cells (such ability of polypeptides of the invention					Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Y Fessen et al., J Biol Chem 268(19):14285- 14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. Assays for the activation of transcription transcription through through the Serum Response Element serum response element (SRE) are well-known in the art and may in immune cells (such ability of polypeptides of the invention					Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
85:6342-6346 (1988); Aramburu et al., J Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285- 14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. Assays for the activation of transcription transcription through the Serum Response Element serum response element (SRE) are well-known in the art and may in immune cells (such ability of polypeptides of the invention ability of polypeptides of the invention					Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
Exp Med 182(3):801-810 (1995); De Boer et al., Int J Biochem Cell Biol 31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. HTXJY08 992 Activation of Assays for the activation of transcription through the Serum Response Element serum response element (SRE) are well-known in the art and may in immune cells (such ability of polypeptides of the invention					85:6342-6346 (1988); Aramburu et al., J	such as, for example, hyperplasia, metaplasia, and/or
HTXJY08 HTX					Exp Med 182(3):801-810 (1995); De Boer	dysplasia. Preferred indications also include anemia,
31(10):1221-1236 (1999); Fraser et al., Eur J Immunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285- 14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. Assays for the activation of transcription transcription through serum response element (SRE) are well-known in the art and may in immune cells (such as natural killer cells). ability of polypeptides of the invention					et al., Int J Biochem Cell Biol	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
Jimmunol 29(3):838-844 (1999); and Yeseen et al., J Biol Chem 268(19):14285-14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. HTXJY08 992 Activation of Assays for the activation of transcription through through the Serum Response Element serum response element (SRE) are well-known in the art and may in immune cells (such as natural killer cells) ability of polypeptides of the invention					31(10):1221-1236 (1999); Fraser et al., Eur	disease, acute lymphocytic anemia (ALL), plasmacytomas,
Yeseen et al., J Biol Chem 268(19):14285- 14293 (1993), the contents of each of which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. Assays for the activation of transcription through the Serum Response Element serum response element (SRE) are well-known in the art and may in immune cells (such as natural killer cells). ability of polypeptides of the invention					J Immunol 29(3):838-844 (1999); and	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
HTXJY08 992 Activation of transcription through the Serum Response Element serum response element serum as natural killer cells.					Yeseen et al., J Biol Chem 268(19):14285-	granulomatous disease, inflammatory bowel disease,
which are herein incorporated by reference in its entirety. NK cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human NK cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity. Activation of Assays for the activation of transcription through the Serum Response Element serum response element (SRE) are well-known in the art and may in immune cells (such as natural killer cells).					14293 (1993), the contents of each of	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
HTXJY08 992 Activation of transcription through the Serum Response Element serum response element as natural killer cells (such and polypeptides of the invention as natural killer cells).					which are herein incorporated by reference	immune reactions to transplanted organs and tissues,
Activation of transcription through the Serum Response Element serum response element in immune cells (such					in its entirety. NK cells that may be used	hemophilia, hypercoagulation, diabetes mellitus,
HTXJY08 992 Activation of transcription through the Serum Response Element serum response element as natural killer cells).					according to these assays are publicly	endocarditis, meningitis, Lyme Disease, asthma and
HTXJY08 992 Activation of transcription through serum response element serum response element as natural killer cells (such as natural killer cells).					available (e.g., through the ATCC).	allergy.
HTXJY08 992 Activation of transcription through transcription through serum response element serum response element as natural killer cells (such as a natural killer cells).					Exemplary human NK cells that may be	
HTXJY08 992 Activation of transcription through transcription through serum response element serum response element as natural killer cell line, which is a human natural line, which is a human natural line with cytolytic and cytotoxic activities.					used according to these assays include the	
HTXJY08 992 Activation of transcription through the Serum Response Element serum response element in immune cells (such as natural killer cells).					NK-YT cell line, which is a human natural	
HTXJY08 992 Activation of Assays for the activation of transcription through through the Serum Response Element serum response element in immune cells (such as natural killer cells).			•		killer cell line with cytolytic and cytotoxic	
HTXJY08 992 Activation of Assays for the activation of transcription transcription through serum response element (SRE) are well-known in the art and may in immune cells (such as natural killer cells).					activity.	
through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention	478	HTXJY08	992	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
(SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention				transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
be used or routinely modified to assess the ability of polypeptides of the invention				serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
ability of polypeptides of the invention				in immune cells (such	be used or routinely modified to assess the	\sim
				as natural killer cells).	ability of polypeptides of the invention	increasing) INF alpha production. Preferred indications

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			(including antibodies and agonists or	include blood disorders (e.g., as described below under
			antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
			serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
			expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
			and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
			related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
			Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
			the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
			modified to test SRE activity of the	immune response. Additional highly preferred indications
			polypeptides of the invention (including	include inflammation and inflammatory disorders, and
			antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
-			the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
			Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
			and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
			368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
			Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
			Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
			3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
	-		12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
			of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
			reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
			be used according to these assays are	pre-neoplastic conditions, such as, for example,
			publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
			ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,
			used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic
			NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,
			killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous
			activity.	disease, inflammatory bowel disease, neutropenia,
		<u>-</u>		neutrophilia, psoriasis, suppression of immune reactions to
				transplanted organs and tissues, hemophilia,
				hypercoagulation, diabetes mellitus, endocarditis,
				meningitis, Lyme Disease, cardiac reperfusion injury, and
				asthma and allergy. An additional preferred indication
				is infection (e.g., an infectious disease as described below
+				under "Infectious Disease").
479 HTXKF95	663	Activation of Skeletal	Kinase assay. Kinase assays, for examplek	Highly preferred indications include endocrine
		Middle Coll Milit	Lin I Milliage assures, 101 Livin signal	מומטותכום להיפי, מז תכזכוות תחומת חוותכו דיוותסכוווור

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Signation Fautway	transduction that regulate cell promeration	Disolucis) alia disolucis of the lineschioskeletal system.
	or differentiation are well known in the art	Preferred indications include neopiastic diseases (e.g., as
	and may be used or routinely modified to	described below under "Hyperproliferative Disorders"),
	assess the ability of polypeptides of the	blood disorders (e.g., as described below under "Immune
	invention (including antibodies and	Activity", "Cardiovascular Disorders", and/or "Blood-
	agonists or antagonists of the invention) to	Related Disorders"), immune disorders (e.g., as described
	promote or inhibit cell proliferation,	below under "Immune Activity"), neural disorders (e.g., as
	activation, and differentiation. Exemplary	described below under "Neural Activity and Neurological
 	assays for ERK kinase activity that may be	Diseases"), and infection (e.g., as described below under
	used or routinely modified to test ERK	"Infectious Disease"). A highly preferred indication
••••	kinase-induced activity of polypeptides of	is diabetes mellitus. An additional highly preferred
	the invention (including antibodies and	indication is a complication associated with diabetes (e.g.,
	agonists or antagonists of the invention)	diabetic retinopathy, diabetic nephropathy, kidney disease
	include the assays disclosed in Forrer et	(e.g., renal failure, nephropathy and/or other diseases and
	al., Biol Chem 379(8-9):1101-1110	disorders as described in the "Renal Disorders" section
	(1998); Le Marchand-Brustel Y, Exp Clin	below), diabetic neuropathy, nerve disease and nerve
	Endocrinol Diabetes 107(2):126-132	damage (e.g., due to diabetic neuropathy), blood vessel
	(1999); Kyriakis JM, Biochem Soc Symp	blockage, heart disease, stroke, impotence (e.g., due to
	64:29-48 (1999); Chang and Karin, Nature	diabetic neuropathy or blood vessel blockage), seizures,
	410(6824):37-40 (2001); and Cobb MH,	mental confusion, drowsiness, nonketotic hyperglycemic-
	Prog Biophys Mol Biol 71(3-4):479-500	hyperosmolar coma, cardiovascular disease (e.g., heart
	(1999); the contents of each of which are	disease, atherosclerosis, microvascular disease,
	herein incorporated by reference in its	hypertension, stroke, and other diseases and disorders as
	entirety. Rat myoblast cells that may be	described in the "Cardiovascular Disorders" section
	used according to these assays are publicly	below), dyslipidemia, endocrine disorders (as described in
	available (e.g., through the ATCC).	the "Endocrine Disorders" section below), neuropathy,
	Exemplary rat myoblast cells that may be	vision impairment (e.g., diabetic retinopathy and
	used according to these assays include L6	blindness), ulcers and impaired wound healing, infection
	cells. L6 is an adherent rat myoblast cell	(e.g., infectious diseases and disorders as described in the
	line, isolated from primary cultures of rat	"Infectious Diseases" section below, especially of the
	thigh muscle, that fuses to form	urinary tract and skin), carpal tunnel syndrome and
	multinucleated myotubes and striated	Dupuytren's contracture). An additional highly
	fibers after culture in differentiation media.	preferred indication is obesity and/or complications
		associated with obesity. Additional highly preferred
		indications include weight loss or alternatively, weight
***************************************		gain. Aditional highly preferred indications are
		complications associated with insulin resistance.

serious cells (such a first and may in immune cells (such a builty of polypeptides of the invention includes a method for stimulating (e.g., as described below under amagonists of the invention of genes in many cell types. Exemplary assays for transcription through the invention includes and agonists or and Malim, Methods in Enzymol 216:362- Berger et al., Gene 66:1-10 (1998); Cullen and Malim, Methods in Enzymol 216:362- Berger et al., Gene 66:1-10 (1998); Cullen and many contined and interpretation of the invention include and modified to test SRE activity of the invention includes and agonists or an agonists or an agonist or an analysis of the invention include and include an antibodies and agonists or an agonist or an analysis of the invention of genes in many cell types. Exemplary assays for transcription through and include antibodies and agonists or antagonists of the invention of including antibodies and agonists or antagonists of the invention of genes in many cell types. Exemplary assays for transcription through antibodies and agonists or antagonists of treating joint damage in patients with rheumatoid arthritis. Highly preferred indications include antibodies and agonists or antagonists of treating joint damage in patients with rheumatoid antibodies and agonists or antagonists of treating joint damage in patients with rheumatoid antibodies and agonists or antagonists of treating joint damage in patients with rheumatoid antibodies and agonists or antagonists of treating joint damage in patients with rheumatoid antibodies and agonists or antagonists of treating joint damage in patients with rheumatoid antibodies and agonist or antagonists of treating joint damage in patients with rheumatoid antibodies and agonists or antagonists of treating joint damage in patients with rheumatoid antibodies and agonist or antagonist of the agonist or antagonist
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			3873 (1994); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the JURKAT cell line, which is a suspension culture of leukemia cells that produce IL-2 when stimulated.	(e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and preneplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
481	HUFCL31	Production of GM-CSF	GM-CSF FMAT. GM-CSF is expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytes- macrophage progenitors and enhances antimicrobial activity in neutrophils, monocytes and macrophage. Additionally, GM-CSF plays an important role in the differentiation of dendritic cells and monocytes, and increases antigen presentation. GM-CSF is considered to be a proinflammatory cytokine. Assays for immunomodulatory proteins that promote the production of GM-CSF are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to	A highly preferred embodiment of the invention includes a method for stimulating the production of GM-CSF. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of GM-CSF. Highly preferred indications include inflammation and inflammatory disorders. An additional highly preferred indication is infection (e.g., as described below under "Infectious Disease". Highly preferred indications include blood disorders (e.g., neutropenia (and the prevention of neutropenia (e.g., in HIV infected patients), and/or as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications also include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional highly preferred indications include asthma. Highly preferred indications include asthma. Highly preferred indications include neoplastic diseases (e.g., leukemia (e.g., acute

				mediate immunomodulation and modulate	lymphoblastic leukemia, and acute myelogenous
				the growth and differentiation of	leukemia), lymphoma (e.g., non-Hodgkin's lymphoma and
				leukocytes. Exemplary assays that test for	Hodgkin's disease), and/or as described below under
				immunomodulatory proteins evaluate the	"Hyperproliferative Disorders"). Highly preferred
				production of cytokines, such as GM-CSF,	indications include neoplasms and cancers, such as,
				and the activation of T cells. Such assays	leukemia, lymphoma, melanoma, and prostate, breast,
				that may be used or routinely modified to	lung, colon, pancreatic, esophageal, stomach, brain, liver
				test immunomodulatory activity of	and urinary cancer. Other preferred indications include
				polypeptides of the invention (including	benign dysproliferative disorders and pre-neoplastic
				antibodies and agonists or antagonists of	conditions, such as, for example, hyperplasia, metaplasia,
				the invention) include the assays disclosed	and/or dysplasia. Highly preferred indications include:
				in Miraglia et al., J Biomolecular	suppression of immune reactions to transplanted organs
				Screening 4:193-204 (1999); Rowland et	and tissues (e.g., bone marrow transplant); accelerating
				al., "Lymphocytes: a practical approach"	myeloid recovery; and mobilizing hematopoietic
				Chapter 6:138-160 (2000); and Ye et al., J	progenitor cells. Preferred indications include boosting
				Leukoc Biol (58(2):225-233, the contents	a T cell-mediated immune response, and alternatively,
				of each of which are herein incorporated	suppressing a T cell-mediated immune response.
				by reference in its entirety. Natural killer	Preferred indications include anemia, pancytopenia,
				cells that may be used according to these	leukopenia, thrombocytopenia, acute lymphocytic anemia
				assays are publicly available (e.g., through	(ALL), plasmacytomas, multiple myeloma, Burkitt's
				the ATCC) or may be isolated using	lymphoma, arthritis, AIDS, granulomatous disease,
				techniques disclosed herein or otherwise	inflammatory bowel disease, sepsis, neutrophilia,
				known in the art. Natural killer (NK) cells	psoriasis, hemophilia, hypercoagulation, diabetes mellitus,
				are large granular lymphocytes that have	endocarditis, meningitis, Lyme Disease, and allergy.
				cytotoxic activity but do bind antigen. NK	
				cells show antibody-independent killing of	
				tumor cells and also recognize antibody	
				bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.	
482 HU	HUKBT67	966	Activation of	Kinase assay. JNK and p38 kinase assays	A highly preferred embodiment of the invention
			Endothelial Cell p38 or	for signal transduction that regulate cell	includes a method for stimulating endothelial cell growth.
-		_	JNK Signaling	proliferation, activation, or apoptosis are	An alternative highly preferred embodiment of the
			Pathway.	well known in the art and may be used or	invention includes a method for inhibiting endothelial cell
		_		routinely modified to assess the ability of	growth. A highly preferred embodiment of the
				polypeptides of the invention (including	invention includes a method for stimulating endothelial
				antibodies and agonists or antagonists of	cell proliferation. An alternative highly preferred
		i i	T	the invention) to promote or initial cell	embounding of the myenion includes a include for

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proliferation, activation, and apoptosis.	-
Exemplary assays for JNK and p38 kinase activity that may be used or routinely	lase preferred embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An
modified to test JNK and p38 kinase-	
induced activity of polypeptides of the	includes a method for inhibiting (e.
invention (including antibodies and	
 agonists or antagonists of the invention)	
include the assays disclosed in Forrer et	
al., Biol Chem 379(8-9):1101-1110	
(1998); Gupta et al., Exp Cell Res 247(2):	
495-504 (1999); Kyriakis JM, Biochem	decreasing) the activation
Soc Symp 64:29-48 (1999); Chang and	
Karin, Nature 410(6824):37-40 (2001);	; the invention includes a method for stimulating
and Cobb MH, Prog Biophys Mol Biol	
71(3-4):479-500 (1999); the contents of	of the invention includes a method for inhibiting
each of which are herein incorporated by	_
reference in its entirety. Endothelial cells	ells invention includes a method for reducing cardiac
that may be used according to these assays	
are publicly available (e.g., through the	of the invention includes a method for inducing cardiac
ATCC). Exemplary endothelial cells that	at
may be used according to these assays	
include human umbilical vein endothelial	ial
cells (HUVEC), which are endothelial	
cells which line venous blood vessels, and	
are involved in functions that include, but	
are not limited to, angiogenesis, vascular	ar atherosclerosis and atherosclerotic vascular disease,
permeability, vascular tone, and immune	
cell extravasation.	hypertrophy, myocardial infarction, chronic hemodynamic
	overload, and/or as described below under
	"Cardiovascular Disorders"). Highly preferred indications
	include cardiovascular, endothelial and/or angiogenic
	disorders (e.g., systemic disorders that affect vessels such
	as diabetes mellitus, as well as diseases of the vessels
	themselves, such as of the arteries, capillaries, veins and/or
	lymphatics). Highly preferred are indications that
	stimulate angiogenesis and/or cardiovascularization.
	Highly preferred are indications that inhibit angiogenesis

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	and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid	tumors, leukemias, and Kaposi's sarcoma, and retinal	disorders. Highly preferred indications include neoplasms	and cancer, such as, Kaposi's sarcoma, hemangioma	(capillary and cavernous), glomus tumors, telangiectasia,	bacillary angiomatosis, hemangioendothelioma,	angiosarcoma, haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver, and urinary	cancer. Preferred indications include benign	dysproliferative disorders and pre-neoplastic conditions,	such as, for example, hyperplasia, metaplasia, and/or	dysplasia. Highly preferred indications also include	arterial disease, such as, atherosclerosis, hypertension,	coronary artery disease, inflammatory vasculitides,	Reynaud's disease and Reynaud's phenomenom,	aneurysms, restenosis; venous and lymphatic disorders	such as thrombophlebitis, lymphangitis, and lymphedema;	and other vascular disorders such as peripheral vascular	disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue	(e.g., vascular injury such as, injury resulting from balloon	angioplasty, and atheroschlerotic lesions), implant	fixation, scarring, ischemia reperfusion injury, rheumatoid	arthritis, cerebrovascular disease, renal diseases such as	acute renal failure, and osteoporosis. Additional highly	preferred indications include stroke, graft rejection,	diabetic or other retinopathies, thrombotic and coagulative	disorders, vascularitis, lymph angiogenesis, sexual	disorders, age-related macular degeneration, and treatment	/prevention of endometriosis and related conditions.	Additional highly preferred indications include fibromas,	heart disease, cardiac arrest, heart valve disease, and	vascular disease. Preferred indications include blood	disorders (e.g., as described below under "Immune
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				Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
483 HUKDF20	766	Regulation of transcription via DMEF1 response element in adipocytes and pre-adipocytes	Assays for the regulation of transcription through the DMEF1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to activate the DMEF1 response element in a reporter construct (such as that containing the GLUT4 promoter) and to regulate insulin production. The DMEF1 response element is present in the GLUT4 promoter and binds to MEF2 transcription factor and another transcription factor that is required for insulin regulation of Glut4 expression in skeletal muscle. GLUT4 is the primary insulin-responsive glucose transporter in fat and muscle tissue. Exemplary assays that may be used or routinely modified to test for DMEF1 response element activity (in adipocytes and pre-adipocytes) by polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed inThai, M.V., et al., J Biol Chem,	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma, cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other diseases and disorders as described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection (e.g., infectious diseases and disorders as described in the "Infectious biseases" section below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). An additional highly preferred indications include nebesity. Additional highly preferred indications include
			273(23):14285-92 (1998); Mora, S., et al., J Biol Chem, 275(21):16323-8 (2000); Liu, M.L., et al., J Biol Chem, 269(45):28514-	weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.

				21 (1994); "Identification of a 30-base pair	
				regulatory element and novel DNA	
				binding protein that regulates the human	
				GLUT4 promoter in transgenic mice", J	
				Biol Chem. 2000 Aug 4;275(31):23666-	
				73; Berger, et al., Gene 66:1-10 (1988);	
				and, Cullen, B., et al., Methods in	
				Enzymol. 216:362-368 (1992), the	
				contents of each of which is herein	
				incorporated by reference in its entirety.	
				Adipocytes and pre-adipocytes that may be	
				used according to these assays are publicly	
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				cells that may be used according to these	
				assays include the mouse 3T3-L1 cell line	
				which is an adherent mouse preadipocyte	
				cell line. Mouse 3T3-L1 cells are a	
				continuous substrain of 3T3 fibroblasts	
				developed through clonal isolation. These	
				cells undergo a pre-adipocyte to adipose-	
	٠			like conversion under appropriate	
				differentiation culture conditions.	
483	HUKDF20	266	Activation of	Assays for the activation of transcription	Preferred indications include neoplastic diseases (e.g.,
			transcription through	through the AP1 response element are	as described below under "Hyperproliferative Disorders"),
			AP1 response element	known in the art and may be used or	blood disorders (e.g., as described below under "Immune
			in immune cells (such	routinely modified to assess the ability of	Activity", "Cardiovascular Disorders", and/or "Blood-
			as T-cells).	polypeptides of the invention (including	Related Disorders"), and infection (e.g., an infectious
				antibodies and agonists or antagonists of	disease as described below under "Infectious Disease").
				the invention) to modulate growth and	Highly preferred indications include autoimmune diseases
				other cell functions. Exemplary assays for	(e.g., rheumatoid arthritis, systemic lupus erythematosis,
				transcription through the AP1 response	multiple sclerosis and/or as described below) and
				element that may be used or routinely	immunodeficiencies (e.g., as described below). Additional
				modified to test AP1-response element	highly preferred indications include inflammation and
				activity of polypeptides of the invention	inflammatory disorders. Highly preferred indications
				(including antibodies and agonists or	also include neoplastic diseases (e.g., leukemia,
				antagonists of the invention) include	lymphoma, and/or as described below under

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"Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below
assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension-culture cell line with cytotoxic activity.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA
	Activation of transcription through serum response element in immune cells (such as T-cells).
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	HUKDF20
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		,		85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, mortional disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
483	HUKDF20	766	Production of ICAM-1	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281 (2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke

				available (e.g. throlloh the ATCC) and/or	
				may be routinely generated. Exemplary	
				cells that may be used according to these	
				assays include microvascular endothelial	
483	HIKDF20	997	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
2			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative highly preferred embodiment of
			in immune cells (such	be used or routinely modified to assess the	the invention includes a method for stimulating (e.g.,
			as natural killer cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
				antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				serum response factors and modulate the	"Cardiovascular Disorders"), Highly preferred indications
				expression of genes involved in growth	include autoimmune diseases (e.g., rheumatoid arthritis,
				and upregulate the function of growth-	systemic lupus erythematosis, Crohn's disease, multiple
				related genes in many cell types.	sclerosis and/or as described below), immunodeficiencies
				Exemplary assays for transcription through	(e.g., as described below), boosting a T cell-mediated
				the SRE that may be used or routinely	immune response, and suppressing a T cell-mediated
			-	modified to test SRE activity of the	immune response. Additional highly preferred indications
				polypeptides of the invention (including	include inflammation and inflammatory disorders, and
				antibodies and agonists or antagonists of	treating joint damage in patients with rheumatoid arthritis.
				the invention) include assays disclosed in	An additional highly preferred indication is sepsis.
				Berger et al., Gene 66:1-10 (1998); Cullen	Highly preferred indications include neoplastic diseases
				and Malm, Methods in Enzymol 216:362-	(e.g., leukemia, lymphoma, and/or as described below
				368 (1992); Henthorn et al., Proc Natl	under "Hyperproliferative Disorders"). Additionally,
				Acad Sci USA 85:6342-6346 (1988);	highly preferred indications include neoplasms and
				Benson et al., J Immunol 153(9):3862-	cancers, such as, for example, leukemia, lymphoma,
				3873 (1994); and Black et al., Virus Genes	melanoma, glioma (e.g., malignant glioma), solid tumors,
				12(2):105-117 (1997), the content of each	and prostate, breast, lung, colon, pancreatic, esophageal,
				of which are herein incorporated by	stomach, brain, liver and urinary cancer. Other preferred
				reference in its entirety. T cells that may	indications include benign dysproliferative disorders and
				be used according to these assays are	pre-neoplastic conditions, such as, for example,
				publicly available (e.g., through the	hyperplasia, metaplasia, and/or dysplasia. Preferred
				ATCC). Exemplary T cells that may be	indications include anemia, pancytopenia, leukopenia,
				used according to these assays include the	thrombocytopenia, Hodgkin's disease, acute lymphocytic
				NK-YT cell line, which is a human natural	anemia (ALL), plasmacytomas, multiple myeloma,
				killer cell line with cytolytic and cytotoxic	Burkitt's lymphoma, arthritis, AIDS, granulomatous

				activity.	disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
484	HUKDY82	866	Activation of transcription through GAS response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al., J Immunol 155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOI T4 cell line, that may be used	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's disease), melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infections, tuberculosis, infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or an infectious disease as described below under "Infectious Disease"). An additional preferred indication is idiopathic pulmonary fibrosis. Preferred indications include angerial lancerical
				according to these assays are publicly	thrombocytopenia, acute lymphocytic anemia (ALL),

				available (e.g., through the ATCC).	plasmacytomas, multiple myeloma, arthritis, AIDS,
					granulomatous disease, inflammatory bowel disease,
					sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues,
					hemophilia, hypercoagulation, diabetes mellitus,
					endocarditis, meningitis, Lyme Disease, and asthma and allergy.
485	HUSCJ14	666	Regulation of	Assays for the regulation of transcription	A highly preferred indication is diabetes mellitus.
			transcription through	through the FAS promoter element are	An additional highly preferred indication is a complication
			the FAS promoter	well-known in the art and may be used or	associated with diabetes (e.g., diabetic retinopathy,
			element in hepatocytes	routinely modified to assess the ability of	diabetic nephropathy, kidney disease (e.g., renal failure,
				polypeptides of the invention (including	nephropathy and/or other diseases and disorders as
				antibodies and agonists or antagonists of	described in the "Renal Disorders" section below), diabetic
				the invention) to activate the FAS	neuropathy, nerve disease and nerve damage (e.g., due to
				promoter element in a reporter construct	diabetic neuropathy), blood vessel blockage, heart disease,
				and to regulate transcription of FAS, a key	stroke, impotence (e.g., due to diabetic neuropathy or
				enzyme for lipogenesis. FAS promoter is	blood vessel blockage), seizures, mental confusion,
				regulated by many transcription factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
				including SREBP. Insulin increases FAS	coma, cardiovascular disease (e.g., heart disease,
				gene transcription in livers of diabetic	atherosclerosis, microvascular disease, hypertension,
				mice. This stimulation of transcription is	stroke, and other diseases and disorders as described in the
				also somewhat glucose dependent.	"Cardiovascular Disorders" section below), dyslipidemia,
				Exemplary assays that may be used or	endocrine disorders (as described in the "Endocrine
				routinely modified to test for FAS	Disorders" section below), neuropathy, vision impairment
				promoter element activity (in hepatocytes)	(e.g., diabetic retinopathy and blindness), ulcers and
				by polypeptides of the invention (including	impaired wound healing, and infection (e.g., infectious
				antibodies and agonists or antagonists of	diseases and disorders as described in the "Infectious
				the invention) include assays disclosed in	Diseases" section below, especially of the urinary tract and
				Xiong, S., et al., Proc Natl Acad Sci	skin), carpal tunnel syndrome and Dupuytren's
				U.S.A., 97(8):3948-53 (2000); Roder, K.,	contracture). An additional highly preferred
				et al., Eur J Biochem, 260(3):743-51	indication is obesity and/or complications associated with
				(1999); Oskouian B, et al., Biochem J, 317	obesity. Additional highly preferred indications include
				(Pt 1):257-65 (1996); Berger, et al., Gene	weight loss or alternatively, weight gain. Aditional
				66:1-10 (1988); and, Cullen, B., et al.,	highly preferred indications are complications associated
				Methods in Enzymol. 216:362–368 (1992),	with insulin resistance.
				the contents of each of which is herein	
				incorporated by reference in its entirety.	

			Hepatocytes that may be used according to these assays, such as H4IIE cells, are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to these assays include rat liver hepatoma cell line(s) inducible with glucocorticoids, insulin, or cAMP derivatives.	
485 HUSCJ14	999	Upregulation of T cells and activation of T cells	CD71 FMAT. CD71 is the transferrin receptor. Transferrin is a major iron carrying protein that is essential for cell proliferation. CD71 is expressed predominantly on cells that are actively proliferating. Assays for immunomodulatory proteins expressed on activated T cells, B cells, and most proliferating cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate the activation of T cells, and/or mediate humoral or cell-mediated immunomodulatory proteins evaluate the upregulation of cell surface markers, such as CD71, and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the assays disclosed in Miraglia et al. I Biomolecular Screening 4:193-204	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. Additional highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperpoliferative Disorders"). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperpoliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperpolastic
			(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's

			(2000); and Afetra et al., Ann Rheum Dis 52(6):457-460 (1993), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T Cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be	disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and asthma and allergy.
HUSGL67	0001	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998), Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below and and and and and and and and a secribed below and a described and a des
			virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T	highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors,

				cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
487	HUSGU40	1001	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al.,	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally,

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			Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
488 HUSIR18	1002	Activation of transcription through serum response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm,	under "Infectious Disease"). A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn's disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis.

488	MISIR 18	1001		Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); and Black et al., Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell line, which is an IL-2 dependent suspension culture of T cells with cytotoxic activity.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
4 8 8	HUSIKI8	7007	Production of IL-10 and downregulation of immune responses	IL-10 FMAT. Assays for immunomodulatory proteins produced by activated T cells, B cells, and monocytes that exhibit anti-inflammatory activity and downregulate monocyte/macrophage function and expression of cytokines are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate inflammatory activities, and modulate immune cell function and cytokine production.	A highly preferred embodiment of the invention includes a method for stimulating the production of IL-10. An alternative preferred embodiment of the invention includes a method for inhibiting the production of IL-10. Highly preferred indications include inflammation and inflammatory disorders (e.g. inflammatory bowel disease). An additional highly preferred indication includes inflammatory bowel disease. Additional highly preferred indications include blood disorders (e.g., as described below under "Immune Activity" (e.g. as ututionmune disorders), "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as

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			Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-10, and the downmodulation of immune responses. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular	described below) and immunodeficiencies (e.g., as described below). Preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
			al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Koning et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Koning et al., Cytokine 9(6):427-436 (1997), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human T cells are primary human lymphocytes that mature in the thymus and express a T cell receptor and CD3, CD4, or CD8. These cells mediate humoral or cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors.	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, Crohn's disease, arthritis, AIDS, granulomatous disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy. An additional preferred indication is infection (e.g., as described below under "Infectious Disease").
489 HUVDJ48 1003)3	Regulation of viability and proliferation of pancreatic beta cells.	Assays for the regulation of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pancreatic beta cells. For example, the Cell Titer-Glo luminescent	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or

				cell viability assay measures the number of	blood vessel blockage), seizures, mental confusion.
				viable cells in culture based on	drowsiness, nonketotic hyperglycemic-hyperosmolar
				quantitation of the ATP present which	coma, cardiovascular disease (e.g., heart disease,
				signals the presence of metabolically	atherosclerosis, microvascular disease, hypertension,
				active cells. Exemplary assays that may be	stroke, and other diseases and disorders as described in the
				used or routinely modified to test	"Cardiovascular Disorders" section below), dyslipidemia,
	***			regulation of viability and proliferation of	endocrine disorders (as described in the "Endocrine
				pancreatic beta cells by polypeptides of the	Disorders" section below), neuropathy, vision impairment
				invention (including antibodies and	(e.g., diabetic retinopathy and blindness), ulcers and
				agonists or antagonists of the invention)	impaired wound healing, and infection (e.g., infectious
				include assays disclosed in: Friedrichsen	diseases and disorders as described in the "Infectious
				BN, et al., Mol Endocrinol, 15(1):136-48	Diseases" section below, especially of the urinary tract and
				(2001); Huotari MA, et al., Endocrinology,	skin), carpal tunnel syndrome and Dupuytren's
				139(4):1494-9 (1998); Hugl SR, et al., J	contracture). An additional highly preferred
				Biol Chem 1998 Jul 10;273(28):17771-9	obesit
				(1998), the contents of each of which is	obesity. Additional highly preferred indications include
				herein incorporated by reference in its	weight loss or alternatively, weight gain. Aditional
				entirety. Pancreatic cells that may be used	tions ass
				according to these assays are publicly	with insulin resistance.
				available (e.g., through the ATCC) and/or	
				may be routinely generated. Exemplary	
				pancreatic cells that may be used	
				according to these assays include rat INS-1	
	• • •			cells. INS-1 cells are a semi-adherent cell	
				line established from cells isolated from an	
				X-ray induced rat transplantable	
				insulinoma. These cells retain	
				characteristics typical of native pancreatic	
				beta cells including glucose inducible	
				insulin secretion. References: Asfari et al.	
				Endocrinology 1992 130:167.	
490	HWAAI12	1004		-	A highly preferred embodiment of the invention
			and activation of T cells	receptor. Transferrin is a major iron	includes a method for stimulating T cell proliferation. An
				carrying protein that is essential for cell	alternative highly preferred embodiment of the invention
				proliferation. CD71 is expressed	includes a method for inhibiting T cell proliferation.
				predominantly on cells that are actively	Preferred indications include blood disorders (e.g., as
				proliferating. Assays for	described below under "Immune Activity", "Blood-

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-			immunomodulatory proteins expressed on	Related Disorders", and/or "Cardiovascular Disorders"),
			activated T cells, B cells, and most	and infection (e.g., as described below under "Infectious
			proliferating cells are well known in the art	Disease"). Highly preferred indications include
			and may be used or routinely modified to	autoimmune diseases (e.g., rheumatoid arthritis, systemic
*******			assess the ability of polypeptides of the	lupus erythematosis, multiple sclerosis and/or as described
			invention (including antibodies and	below), immunodeficiencies (e.g., as described below),
			agonists or antagonists of the invention) to	boosting a T cell-mediated immune response, and
			modulate the activation of T cells, and/or	suppressing a T cell-mediated immune response.
			mediate humoral or cell-mediated	Additional highly preferred indications include
			immunity. Exemplary assays that test for	inflammation and inflammatory disorders. Additional
			immunomodulatory proteins evaluate the	highly preferred indications include infection. Preferred
			upregulation of cell surface markers, such	indications include neoplastic diseases (e.g., leukemia,
			as CD71, and the activation of T cells.	lymphoma, and/or as described below under
			Such assays that may be used or routinely	"Hyperproliferative Disorders"). Preferred indications
			modified to test immunomodulatory	include neoplasms and cancers, such as, for example,
•			activity of polypeptides of the invention	leukemia, lymphoma, melanoma, and prostate, breast,
			(including antibodies and agonists or	lung, colon, pancreatic, esophageal, stomach, brain, liver
			antagonists of the invention) include, for	and urinary cancer. Other preferred indications include
			example, the assays disclosed in Miraglia	benign dysproliferative disorders and pre-neoplastic
			et al., J Biomolecular Screening 4:193-204	conditions, such as, for example, hyperplasia, metaplasia,
			(1999); Rowland et al., "Lymphocytes: a	and/or dysplasia. Preferred indications include anemia,
			practical approach" Chapter 6:138-160	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
			(2000); and Afetra et al., Ann Rheum Dis	disease, acute lymphocytic anemia (ALL), plasmacytomas,
			52(6):457-460 (1993), the contents of each	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
			of which are herein incorporated by	granulomatous disease, inflammatory bowel disease,
			reference in its entirety. Human T cells	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
			that may be used according to these assays	immune reactions to transplanted organs and tissues,
			may be isolated using techniques disclosed	hemophilia, hypercoagulation, diabetes mellitus,
			herein or otherwise known in the art.	endocarditis, meningitis, Lyme Disease, and asthma and
			Human T cells are primary human	allergy.
			lymphocytes that mature in the thymus and	
			express a T Cell receptor and CD3, CD4,	
			or CD8. These cells mediate humoral or	
			cell-mediated immunity and may be	
			preactivated to enhance responsiveness to	
			immunomodulatory factors.	
HWBBQ70	1005	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
IOI	370		1005 Production of II	and may be used or routinely modified to assess the ability of polypeptides of the invention) to modulate the activation of reells, and/or mediate thumoral or cell-mediated immunity. Exemplary assays that test for immunity. Exemplary assays that test for immunity. Exemplary assays that test for immunity. Exemplary assays that east for immunity. Exemplary assays that test for immunity. Exemplary assays that test for immunity. Exemplary assays that test for immunity. Exemplary assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include, for example, the assays disclosed in Miraglia et al., 4 Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:183-160 (2000); and Afetra et al., Ann Rheum Dis 52(6):457-460 (1993), the contents of each of which are herein incorporated by reference in its entirety. Human T cells that may be used according to these assays or Cell-mediated immunity and may be preactivated to enhance responsiveness to immunomodulatory factors. 1005 Production of IL-6 is produced by T cells

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and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
 cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal
of IL-6 has been linked to autoimmune	immunity. Highly preferred indications include blood
disease, plasmacytomas, myelomas, and	disorders (e.g., as described below under "Immune
chronic hyperproliferative diseases.	Activity", "Blood-Related Disorders", and/or
Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
or routinely modified to assess the ability	preferred indications also include boosting a B cell-
of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
the invention) to mediate	indications include inflammation and inflammatory
immunomodulation and differentiation and	disorders. Additional highly preferred indications include
modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
 Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
 158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
each of which are herein incorporated by	transplanted organs and tissues, hemophilia,

492 HWBCN36 1006 Production of ICAM-1	presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
1006	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
	assess the ability of polypeptides of the	and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, Restenosis, and Stroke
	invention (including antibodies and	
	agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary	
	assays that may be used or routinely modified to measure ICAM-1 expression	
	include assays disclosed in: Takacs P, et al,	
	FASEB J, 15(2):279-281 (2001); and, Mivamoto K. et al., Am J Pathol.	
	156(5):1733-1739 (2000), the contents of	
	each of which is herein incorporated by	
	reference in its entirety. Cells that may be	
	used according to these assays are publicly	
	available (e.g., unough me A1CC) and on may be routinely generated Exemplary	
	cells that may be used according to these	
	assays include microvascular endothelial	
	cells (MVEC).	
HWBDJ08 1007 Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells	A highly preferred embodiment of the invention
	and has strong effects on B cells. IL-6	includes a method for stimulating (e.g., increasing) IL-6
	participates in IL-4 induced IgE production	production. An alternative highly preferred embodiment of
	and increases IgA production (IgA plays a	the invention includes a method for inhibiting (e.g.,
	role in mucosal immunity). IL-6 induces	reducing) IL-6 production. A highly preferrred
	cytotoxic T cells. Deregulated expression	indication is the stimulation or enhancement of mucosal

		discussion (a se or decombed heless made "(Tenenson
	chronic hypermoliferative diseases.	Activity", "Blood-Related Disorders", and/or
	Assays for immunomodulatory and	"Cardiovascular Disorders"), and infection (e.g., as
	differentiation factor proteins produced by	described below under "Infectious Disease"). Highly
	a large variety of cells where the	preferred indications include autoimmune diseases (e.g.,
	expression level is strongly regulated by	rheumatoid arthritis, systemic lupus erythematosis,
	cytokines, growth factors, and hormones	multiple sclerosis and/or as described below) and
	are well known in the art and may be used	immunodeficiencies (e.g., as described below). Highly
	or routinely modified to assess the ability	preferred indications also include boosting a B cell-
	of polypeptides of the invention (including	mediated immune response and alternatively suppressing a
	antibodies and agonists or antagonists of	B cell-mediated immune response. Highly preferred
	the invention) to mediate	indications include inflammation and inflammatory
	immunomodulation and differentiation and	disorders. Additional highly preferred indications include
	modulate T cell proliferation and function.	asthma and allergy. Highly preferred indications include
	Exemplary assays that test for	neoplastic diseases (e.g., myeloma, plasmacytoma,
	immunomodulatory proteins evaluate the	leukemia, lymphoma, melanoma, and/or as described
	production of cytokines, such as IL-6, and	below under "Hyperproliferative Disorders"). Highly
	the stimulation and upregulation of T cell	preferred indications include neoplasms and cancers, such
	proliferation and functional activities.	as, myeloma, plasmacytoma, leukemia, lymphoma,
	Such assays that may be used or routinely	melanoma, and prostate, breast, lung, colon, pancreatic,
	modified to test immunomodulatory and	esophageal, stomach, brain, liver and urinary cancer.
	diffferentiation activity of polypeptides of	Other preferred indications include benign dysproliferative
	the invention (including antibodies and	disorders and pre-neoplastic conditions, such as, for
	agonists or antagonists of the invention)	example, hyperplasia, metaplasia, and/or dysplasia.
	include assays disclosed in Miraglia et al.,	Preferred indications include anemia, pancytopenia,
	J Biomolecular Screening 4:193-	leukopenia, thrombocytopenia, Hodgkin's disease, acute
	204(1999); Rowland et al., "Lymphocytes:	lymphocytic anemia (ALL), multiple myeloma, Burkitt's
	a practical approach" Chapter 6:138-160	lymphoma, arthritis, AIDS, granulomatous disease,
	(2000); and Verhasselt et al., J Immunol	inflammatory bowel disease, sepsis, neutropenia,
	158:2919-2925 (1997), the contents of	neutrophilia, psoriasis, suppression of immune reactions to
	each of which are herein incorporated by	transplanted organs and tissues, hemophilia,
	reference in its entirety. Human dendritic	hypercoagulation, diabetes mellitus, endocarditis,
-	cells that may be used according to these	meningitis, and Lyme Disease. An additional preferred
	assays may be isolated using techniques	indication is infection (e.g., an infectious disease as
	disclosed herein or otherwise known in the	described below under "Infectious Disease").
	art. Human dendritic cells are antigen	
	presenting cells in suspension culture,	

				which, when activated by antigen and/or cytokines, initiate and upregulate T cell	
				proliferation and functional activities.	
493	HWBDJ08	1007	Activation of	Assays for the activation of transcription	Highly preferred indications include blood disorders
			transcription through	through the Nuclear Factor of Activated T	(e.g., as described below under "Immune Activity",
			NFAT response	cells (NFAT) response element are well-	"Blood-Related Disorders", and/or "Cardiovascular
			element in immune	known in the art and may be used or	Disorders"). Highly preferred indications include
			cells (such as T-cells).	routinely modified to assess the ability of	autoimmune diseases (e.g., rheumatoid arthritis, systemic
			,	polypeptides of the invention (including	lupus erythematosis, multiple sclerosis and/or as described
				antibodies and agonists or antagonists of	below), immunodeficiencies (e.g., as described below),
				the invention) to regulate NFAT	boosting a T cell-mediated immune response, and
				transcription factors and modulate	suppressing a T cell-mediated immune response.
		٠		expression of genes involved in	Additional highly preferred indications include
				immunomodulatory functions. Exemplary	inflammation and inflammatory disorders. An additional
				assays for transcription through the NFAT	highly preferred indication is infection (e.g., an infectious
				response element that may be used or	disease as described below under "Infectious Disease").
				routinely modified to test NFAT-response	Preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Preferred indications
				agonists or antagonists of the invention)	include neoplasms and cancers, such as, for example,
				include assays disclosed in Berger et al.,	leukemia, lymphoma, and prostate, breast, lung, colon,
				Gene 66:1-10 (1998); Cullen and Malm,	pancreatic, esophageal, stomach, brain, liver and urinary
				Methods in Enzymol 216:362-368 (1992);	cancer. Other preferred indications include benign
				Henthorn et al., Proc Natl Acad Sci USA	dysproliferative disorders and pre-neoplastic conditions,
				85:6342-6346 (1988); Serfling et al.,	such as, for example, hyperplasia, metaplasia, and/or
				Biochim Biophys Acta 1498(1):1-18	dysplasia. Preferred indications also include anemia,
				(2000); De Boer et al., Int J Biochem Cell	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				Biol 31(10):1221-1236 (1999); Fraser et	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				al., Eur J Immunol 29(3):838-844 (1999);	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
				and Yeseen et al., J Biol Chem	granulomatous disease, inflammatory bowel disease,
				268(19):14285-14293 (1993), the contents	sepsis, neutropenia, neutrophilia, psoriasis, suppression of
				of each of which are herein incorporated	immune reactions to transplanted organs and tissues,
				by reference in its entirety. T cells that	hemophilia, hypercoagulation, diabetes mellitus,
				may be used according to these assays are	endocarditis, meningitis, Lyme Disease, asthma and
				publicly available (e.g., through the	allergy.
				ATCC). Exemplary human T cells that	
				may be used according to these assays	

				include the SUPT cell line, which is a suspension culture of II -2 and II -4	
				responsive T cells.	
494 HW	HWBFX16	1008	Activation of	Assays for the activation of transcription	Preferred indications include blood disorders (e.g., as
			transcription through	through the cAMP response element are	described below under "Immune Activity", "Blood-
			cAMP response	well-known in the art and may be used or	Related Disorders", and/or "Cardiovascular Disorders"),
	-		element in immune	routinely modified to assess the ability of	and infection (e.g., an infectious disease as described
			cells (such as T-cells).	polypeptides of the invention (including	below under "Infectious Disease"). Preferred
				antibodies and agonists or antagonists of	indications include autoimmune diseases (e.g., rheumatoid
				the invention) to increase cAMP, regulate	arthritis, systemic lupus erythematosis, multiple sclerosis
	_			CREB transcription factors, and modulate	and/or as described below), immunodeficiencies (e.g., as
				expression of genes involved in a wide	described below), boosting a T cell-mediated immune
				variety of cell functions. Exemplary	response, and suppressing a T cell-mediated immune
				assays for transcription through the cAMP	response. Additional preferred indications include
				response element that may be used or	inflammation and inflammatory disorders. Highly
				routinely modified to test cAMP-response	preferred indications include neoplastic diseases (e.g.,
				element activity of polypeptides of the	leukemia, lymphoma, and/or as described below under
				invention (including antibodies and	"Hyperproliferative Disorders"). Highly preferred
				agonists or antagonists of the invention)	indications include neoplasms and cancers, such as, for
				include assays disclosed in Berger et al.,	example, leukemia, lymphoma (e.g., T cell lymphoma,
				Gene 66:1-10 (1998); Cullen and Malm,	Burkitt's lymphoma, non-Hodgkins lymphoma, Hodgkin's
				Methods in Enzymol 216:362-368 (1992);	disease), melanoma, and prostate, breast, lung, colon,
•				Henthorn et al., Proc Natl Acad Sci USA	pancreatic, esophageal, stomach, brain, liver and urinary
				85:6342-6346 (1988); Black et al., Virus	cancer. Other preferred indications include benign
-				Genes 15(2):105-117 (1997); and	dysproliferative disorders and pre-neoplastic conditions,
				Belkowski et al., J Immunol 161(2):659-	such as, for example, hyperplasia, metaplasia, and/or
-				665 (1998), the contents of each of which	dysplasia. Preferred indications include anemia,
				are herein incorporated by reference in its	pancytopenia, leukopenia, thrombocytopenia, acute
				entirety. T cells that may be used	lymphocytic anemia (ALL), plasmacytomas, multiple
				according to these assays are publicly	myeloma, arthritis, AIDS, granulomatous disease,
				available (e.g., through the ATCC).	inflammatory bowel disease, sepsis, neutropenia,
				Exemplary mouse T cells that may be used	neutrophilia, psoriasis, suppression of immune reactions to
				according to these assays include the HT2	transplanted organs and tissues, hemophilia,
				cell line, which is a suspension culture of	hypercoagulation, diabetes mellitus, endocarditis,
				IL-2 dependent T cells that also respond to	meningitis, Lyme Disease, and asthma and allergy.
+				114.	
495 HW	HWDAC26	1009	Activation of	Kinase assay. JNK kinase assays for	A highly preferred embodiment of the invention includes

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a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An			highly preferred embodiment of the invention incl method for inhibiting the activation of and/or inac endothelial cells. A highly preferred embod the invention includes a method for stimulating angiogenisis. An alternative highly preferred embo of the invention includes a method for inhibiting		failure, hypertension, aortic stenosis, cardiomyopathy, d valvular regurgitation, left ventricular dysfunction, t atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under	"Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect
signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of prolymentides of the invention (including	antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity	that may be used or routinely modified to test JNK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed	in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays	include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	
Endothelial Cell JNK Signaling Pathway.						

		wassals such as diabates mellitus as well as diseases of the	_
		vessels themselves, such as of the arteries, capillaries,	
		veins and/or lymphatics). Highly preferred are indications	
		that stimulate angiogenesis and/or cardiovascularization.	
		Highly preferred are indications that inhibit angiogenesis	
		and/or cardiovascularization. Highly preferred	
		indications include antiangiogenic activity to treat solid	
		tumors, leukemias, and Kaposi's sarcoma, and retinal	
		disorders. Highly preferred indications include neoplasms	
		and cancer, such as, Kaposi's sarcoma, hemangioma	
	•	(capillary and cavernous), glomus tumors, telangiectasia,	
		bacillary angiomatosis, hemangioendothelioma,	
		angiosarcoma, haemangiopericytoma, lymphangioma,	
		lymphangiosarcoma. Highly preferred indications also	
		include cancers such as, prostate, breast, lung, colon,	
		pancreatic, esophageal, stomach, brain, liver, and urinary	
		cancer. Preferred indications include benign	
		dysproliferative disorders and pre-neoplastic conditions,	
		such as, for example, hyperplasia, metaplasia, and/or	
		dysplasia. Highly preferred indications also include	
		arterial disease, such as, atherosclerosis, hypertension,	
		coronary artery disease, inflammatory vasculitides,	
		Reynaud's disease and Reynaud's phenomenom,	
		aneurysms, restenosis; venous and lymphatic disorders	
 		such as thrombophlebitis, lymphangitis, and lymphedema;	
		and other vascular disorders such as peripheral vascular	
		disease, and cancer. Highly preferred indications also	
		include trauma such as wounds, burns, and injured tissue	
		(e.g., vascular injury such as, injury resulting from balloon	
		angioplasty, and atheroschlerotic lesions), implant	
		fixation, scarring, ischemia reperfusion injury, rheumatoid	
		al d	
		acute renal failure, and osteoporosis. Additional highly	
		preferred indications include stroke, graft rejection,	
		diabetic or other retinopathies, thrombotic and coagulative	
		disorders, vascularitis, lymph angiogenesis, sexual	
		disorders, age-related macular degeneration, and treatment	 1

496 HWI	HWDAG96	1010	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the API response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the API response element that may be used or routinely	Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory diseases, e.g., inflammatory bowel disease and Crohn's diseases, e.g., inflammatory bowel disease and Crohn's diseases, and pain management. Preferred indications include neoplastic diseases (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional immunodeficiencies (e.g., as described below). Additional immunodeficiencies (e.g., as described below).
				modified to test APT-response etement activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1988); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Rellahan et al., J Biol Chem 272(49):30806-30811 (1997); Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the	inflammatory disorders. Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia,

				contents of each of which are herein	thrombocytopenia. Hodgkin's disease, acute lymphocytic
				incorporated by reference in its entirety.	anemia (ALL), plasmacytomas, multiple myeloma,
				Mouse T cells that may be used according	Burkitt's lymphoma, granulomatous disease, inflammatory
				to these assays are publicly available (e.g.,	bowel disease, sepsis, psoriasis, suppression of immune
				through the ATCC). Exemplary mouse T	reactions to transplanted organs and tissues, endocarditis,
				cells that may be used according to these	meningitis, and Lyme Disease.
				assays include the HT2 cell line, which is	
			•	an IL-2 dependent suspension culture cell	
				line that also responds to IL-4.	
497	HWDAJ01	1011	Activation of	Assays for the activation of transcription	A preferred embodiment of the invention includes a
			transcription through	through the Serum Response Element	method for inhibiting (e.g., reducing) TNF alpha
			serum response element	(SRE) are well-known in the art and may	production. An alternative preferred embodiment of the
			in immune cells (such	be used or routinely modified to assess the	invention includes a method for stimulating (e.g.,
			as T-cells).	ability of polypeptides of the invention	increasing) TNF alpha production. Preferred indications
				(including antibodies and agonists or	include blood disorders (e.g., as described below under
			-,-	antagonists of the invention) to regulate	"Immune Activity", "Blood-Related Disorders", and/or
				the serum response factors and modulate	"Cardiovascular Disorders"), Highly preferred indications
				the expression of genes involved in	include autoimmune diseases (e.g., rheumatoid arthritis,
				growth. Exemplary assays for	systemic lupus erythematosis, Crohn's disease, multiple
				transcription through the SRE that may be	sclerosis and/or as described below), immunodeficiencies
				used or routinely modified to test SRE	(e.g., as described below), boosting a T cell-mediated
				activity of the polypeptides of the	immune response, and suppressing a T cell-mediated
				invention (including antibodies and	immune response. Additional highly preferred indications
				agonists or antagonists of the invention)	include inflammation and inflammatory disorders, and
				include assays disclosed in Berger et al.,	treating joint damage in patients with rheumatoid arthritis.
				Gene 66:1-10 (1998); Cullen and Malm,	An additional highly preferred indication is sepsis.
				Methods in Enzymol 216:362-368 (1992);	Highly preferred indications include neoplastic diseases
				Henthorn et al., Proc Natl Acad Sci USA	(e.g., leukemia, lymphoma, and/or as described below
				85:6342-6346 (1988); and Black et al.,	under "Hyperproliferative Disorders"). Additionally,
				Virus Genes 12(2):105-117 (1997), the	highly preferred indications include neoplasms and
				content of each of which are herein	cancers, such as, for example, leukemia, lymphoma,
				incorporated by reference in its entirety. T	melanoma, glioma (e.g., malignant glioma), solid tumors,
				cells that may be used according to these	and prostate, breast, lung, colon, pancreatic, esophageal,
				assays are publicly available (e.g., through	stomach, brain, liver and urinary cancer. Other preferred
				the ATCC). Exemplary mouse T cells that	indications include benign dysproliferative disorders and
				may be used according to these assays	pre-neoplastic conditions, such as, for example,
				include the CTLL cell line, which is an IL-	hyperplasia, metaplasia, and/or dysplasia. Preferred

				2 dependent suspension culture of T cells with cytotoxic activity.	indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic
					anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous
					disease, inflammatory bowel disease, neutropenia,
					transplanted organs and tissues, hemophilia,
					hypercoagulation, diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, cardiac reperfusion injury, and
					asthma and allergy. An additional preferred indication
					is infection (e.g., an infectious disease as described below under "Infectious Disease").
498	HWHPB78	1012	Activation of	Assays for the activation of transcription	Highly preferred indications include inflammation and
			transcription through	through the NFKB response element are	inflammatory disorders. Highly preferred indications
			NFKB response	well-known in the art and may be used or	include blood disorders (e.g., as described below under
		****	element in immune	routinely modified to assess the ability of	"Immune Activity", "Blood-Related Disorders", and/or
			cells (such as natural	polypeptides of the invention (including	"Cardiovascular Disorders"). Highly preferred indications
			killer cells).	antibodies and agonists or antagonists of	include autoimmune diseases (e.g., rheumatoid arthritis,
				the invention) to regulate NFKB	systemic lupus erythematosis, multiple sclerosis and/or as
		-		transcription factors and modulate	described below), and immunodeficiencies (e.g., as
				expression of immunomodulatory genes.	described below). An additional highly preferred
				Exemplary assays for transcription through	indication is infection (e.g., AIDS, and/or an infectious
				the NFKB response element that may be	disease as described below under "Infectious Disease").
				used or rountinely modified to test NFKB-	Highly preferred indications include neoplastic diseases
				response element activity of polypeptides	(e.g., melanoma, leukemia, lymphoma, and/or as described
				of the invention (including antibodies and	below under "Hyperproliferative Disorders"). Highly
				agonists or antagonists of the invention)	preferred indications include neoplasms and cancers, such
				include assays disclosed in Berger et al.,	as, for example, melanoma, renal cell carcinoma,
				Gene 66:1-10 (1998); Cullen and Malm,	leukemia, lymphoma, and prostate, breast, lung, colon,
				Methods in Enzymol 216:362-368 (1992);	pancreatic, esophageal, stomach, brain, liver and urinary
				Henthorn et al., Proc Natl Acad Sci USA	cancer. Other preferred indications include benign
				85:6342-6346 (1988); Valle Blazquez et	dysproliferative disorders and pre-neoplastic conditions,
				al, Immunology 90(3):455-460 (1997);	such as, for example, hyperplasia, metaplasia, and/or
				Aramburau et al., J Exp Med 82(3):801-	dysplasia. Preferred indications also include anemia,
				810 (1995); and Fraser et al., 29(3):838-	pancytopenia, leukopenia, thrombocytopenia, Hodgkin's
				844 (1999), the contents of each of which	disease, acute lymphocytic anemia (ALL), plasmacytomas,
				are herein incorporated by reference in its	multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,

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				entirety. NK cells that may be used	granulomatous disease, inflammatory bowel disease,
				according to these assays are publicly	sepsis, neutropenia, neutrophilia, psoriasis, hemophilia,
				avanatic (c.g., unough the ATCC). Exemplary NK cells that may be used	inypercoaguiation, diapetes inclinius, endocalums, meningitis, Lyme Disease, suppression of immune
				according to these assays include the NK-	reactions to transplanted organs, asthma and allergy.
				YT cell line, which is a human natural	
				killer cell line with cytolytic and cytotoxic	
				activity.	
499	HYABC84	1013	Stimulation of Calcium	Assays for measuring calcium flux are	A highly preferred indication is diabetes mellitus.
			Flux in pancreatic beta	well-known in the art and may be used or	An additional highly preferred indication is a complication
			cells.	routinely modified to assess the ability of	associated with diabetes (e.g., diabetic retinopathy,
				polypeptides of the invention (including	diabetic nephropathy, kidney disease (e.g., renal failure,
				antibodies and agonists or antagonists of	nephropathy and/or other diseases and disorders as
				the invention) to mobilize calcium. For	described in the "Renal Disorders" section below), diabetic
				example, the FLPR assay may be used to	neuropathy, nerve disease and nerve damage (e.g., due to
				measure influx of calcium. Cells normally	diabetic neuropathy), blood vessel blockage, heart disease,
				have very low concentrations of cytosolic	stroke, impotence (e.g., due to diabetic neuropathy or
				calcium compared to much higher	blood vessel blockage), seizures, mental confusion,
				extracellular calcium. Extracellular factors	drowsiness, nonketotic hyperglycemic-hyperosmolar
				can cause an influx of calcium, leading to	coma, cardiovascular disease (e.g., heart disease,
				activation of calcium responsive signaling	atherosclerosis, microvascular disease, hypertension,
				pathways and alterations in cell functions.	stroke, and other diseases and disorders as described in the
				Exemplary assays that may be used or	"Cardiovascular Disorders" section below), dyslipidemia,
				routinely modified to measure calcium flux	endocrine disorders (as described in the "Endocrine
				by polypeptides of the invention (including	Disorders" section below), neuropathy, vision impairment
				antibodies and agonists or antagonists of	(e.g., diabetic retinopathy and blindness), ulcers and
				the invention) include assays disclosed in:	impaired wound healing, and infection (e.g., infectious
				Satin LS, et al., Endocrinology,	diseases and disorders as described in the "Infectious
				136(10):4589-601 (1995);Mogami H, et	Diseases" section below, especially of the urinary tract and
				al., Endocrinology, 136(7):2960-6 (1995);	skin), carpal tunnel syndrome and Dupuytren's
				Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
				3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
				Cell Calcium 1989 Nov-Dec;10(8):535-41	obesity. Additional highly preferred indications include
				(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
				herein incorporated by reference in its	highly preferred indications are complications associated
				entirety. Pancreatic cells that may be used	with insulin resistance.
				according to these assays are publicly	

available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santere et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.	Assays for measuring calcium flux are rand may be used or cells. Flux in pancreatic beta continely modified to assess the ability of calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic activation of calcium compared to much higher can cause an influx of calcium. Extracellular factors and agonists or antagonists of the invention) including antibodies and agonists or antagonists of the invention including by polypeptides of the invention including antibodies and agonists or antagonists of the invention including by polypeptides of the invention of calcium cancined agonists or antagonists of the invention including antibodies and agonists or antagonists of the invention include assays that may be used to activation of calcium captures and agonists or antagonists of the invention including and agonists or antagonists of the invention include assays disclosed in the invention include assays disclosed in the invention of capture and agonists or antagonists of the invention of capture and agonists or antagonists of the invention of capture and agonists or antagonists of the invention of capture and agonists or antagonists of the invention of capture and agonists or antagonists of impaired wound healing and infection (e.g., infectious disease, and disorders as described in the "Infectious disease, capture and alterations in cell functions." A highly preferred indication is a complication of action in the art and may be used to measure calcium flux of calcium. Extracellular factors and agonists or antagonists of the invention including and infection (e.g., indepetical captures, indepetical
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	Richardson SB, et al., Biochem J, 288 (Pt	contracture). An additional highly preferred
-	3):847-51 (1992); and, Meats, JE, et al.,	indication is obesity and/or complications associated with
	Cell Calcium 1989 Nov-Dec;10(8):535-41	obesity. Additional highly preferred indications include
	(1989), the contents of each of which is	weight loss or alternatively, weight gain. Aditional
	herein incorporated by reference in its	highly preferred indications are complications associated
	entirety. Pancreatic cells that may be used	with insulin resistance.
	according to these assays are publicly	
	available (e.g., through the ATCC) and/or	
	may be routinely generated. Exemplary	
	pancreatic cells that may be used	
	according to these assays include HITT15	
	Cells. HITT15 are an adherent epithelial	
	cell line established from Syrian hamster	
	islet cells transformed with SV40. These	
	cells express glucagon, somatostatin, and	
	glucocorticoid receptors. The cells secrete	
	insulin, which is stimulated by glucose and	
	glucagon and suppressed by somatostatin	•
	or glucocorticoids. ATTC# CRL-1777	
	Refs: Lord and Ashcroft. Biochem. J. 219:	
	547-551; Santerre et al. Proc. Natl. Acad.	
	Sci. USA 78: 4339-4343, 1981.	

TABLE 2

Clone ID	Contig ID:	SEO	Analysis	PFam/NR Description	PFam/NR Accession	Score/	NT From	NT To
)	U) NO:X	Method	•	Number	Percent Identity		
H6BSF56	762968	11	HMMER 2.1.1	PFAM: Zinc-binding dehydrogenases	PF00107	35.6	176	415
			blastx.2	CGI-63 PROTEIN.	sp Q9Y373 Q9Y373	94%	53	427
					•	72%	48	80
						44%	25	78
H6EDM64	841331	12	blastx.2	ANG2.	saineo saineo ds	%66	922	2451
						100%	107	922
						35%	2235	2459
						34%	874	1038
						36%	203	310
H6EEC72	889401	13	blastx.2	hypothetical protein	pir T43456 T43456	21%	1459	365
				DKFZp434L061.1 - human		20%	1448	807
						%59	1484	927
						53%	137	96
HACBS22	847113	16	blastx.2	adenylate cyclase (EC 4.6.1.1)	pir A39833 A39833	93%	416	2446
				type III - rat		%66	9	416
_						31%	2078	2299
						25%	1445	1987
						23%	917	1111
HADDE71	839187	17	blastx.2	(AP002460)	dbj BAA97098.1	91%	667	999
				gene_id:F1D9.26~unknown		%08	480	999
				protein [Arabidopsis thaliana]		%06	909	199
						100%	520	999
						100%	520	999
						100%	520	999
						100%	520	999
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						100%	520	999
						100%	520	999

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1000	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
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%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	<i>1</i> %96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96
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516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	516	515	520	516	515	1882	1116	1265	1222 1
%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	%96	296	%96	%96	%96	%96	%96	%96	<u> </u> %96	%96	%96	%96	%96	%96	94%	95%	95%	806	42%	27%	%65	100%
																															sp Q14287 Q14287		sp BAB13911 BAB13911	sp Q9NWT5 Q9NWT5
																															HYPOTHETICAL PROTEIN	(FRAGMENT).	CDNA FLJ11786 fis, clone HEMBA1006036.	CDNA FLJ20618 FIS, CLONE KAT05049.
																															blastx.2		blastx.2	blastx.2
																															18		21	22
	<u>.</u>		••••	_	_	_	_																								827273		637489	823543
																													. —		HADDJ13		HAGDW20	HAGEG10

HAGFS57	847120	24	blastx.2	X-LIKE 1 PROTEIN.	sp 09Y485 09Y485	58%	6	872
HAGHN57	773286	25	blastx.2	MITOCHONDRIAL	sp O75439 MPPB_HUM	%86	99	1444
				PROCESSING PEPTIDASE	AN	%66	68	1444
				BETA SUBUNIT PRECURSOR 1		100%	39	68
HAHEA15	847013	26	blastx.2	HYPOTHETICAL 31.4 KDA	sp Q9NWD5 Q9NWD5	%66	30	995
				PROTEIN.		292	455	832
HAJAA47	534670	27	blastx.2	CDA14.	sp Q9NZA3 Q9NZA3	100%	17	157
HAJAY92	845601	28	blastx.2	ORF2-LIKE PROTEIN	sp 000549 000549	31%	1721	2242
				(FRAGMENT).		52%	2226	2333
						39%	1602	1769
						25%	199	915
HAJBV67	866415	29	blastx.2	SM-11044 BINDING	sp Q9UHW8 Q9UHW8	%66	116	1891
				PROTEIN (FRAGMENT).		100%	13	126
HAOAG15	852204	31	HIMMER	PFAM: von Willebrand factor	PF00092	180.1	909	1057
			2.1.1	type A domain				
			blastx.2	INTEGRIN ALPHA-10 PRECURSOR.	sp 075578 ITAG_HUMA N	%86	8	3508
HAQCE11	633730	33	blastx.2	(AY012159) virion-associated	gb AAG42155.1	%96	48	134
	••			nuclear-shuttling protein [Mus musculus]		32%	464	547
HATCI03	580805	37	blastx.2	CDNA: FLJ21463 fis, clone COL04765.	sp BAB15071 BAB15071	%89	924	889
HBAGD86	838799	39	blastx.2	HYPOTHETICAL PROTEIN (FRAGMENT).	sp Q14287 Q14287	37%	801	559
HBDAB91	789532	41	blastx.2	PUTATIVE P150.	sp O00370 O00370	36%	529	5
						40%	587	513
HBDAB91	864374	42	blastx.2	PUTATIVE P150.	sp O00370 O00370	36%	849	307
						40%	206	833
HBGBC29	691473	43	blastx.2	BETA-1,4-	sp 060513 060513	%86	99	1021
				GALACTOSYLIKANSFEKA SE.		 %00I	-	<u>~~</u> 8/
HBHAA05	603174	45	blastx.2	PRO2550.	sp AAG35515 AAG35515	71%	929	386
HBHAA81	846465	46	blastx.2	CDNA FLJ10724 FIS, CLONE NT2RP3001176.	sp Q9NVH9 Q9NVH9	27% 35%	49	1356
HBIAC29	831751	48	blastx.2	CDNA FLJ11730 fis, clone	sp BAB13898 BAB13898	100%	25	597

				1625	790 867	613 1587		- 5		1322 1519		1509 1532	2 1075	285 491	321 551	9 617		8 1528	814 518		809 586						54 941	1.1
	100%	38%	35%	28%	36.6	%66	100%	22%	92%	%68	93%	100%	%99	%86	162.6	95%		%66	75%	44%	47%	61%	24%	44%	53%	%99	100%	100%
	sp Q9NXT6 Q9NXT6				PF00400	splQ9UJD5 Q9UJD5	-		dbj BAB27367.1					sp 095297 095297	PF00510	splP00414 COX3 HUMA	Z	sp Q9NXS4 Q9NXS4	sp BAB15071 BAB15071	sp Q14288 Q14288							sp BAB15583 BAB15583	embly AB66777 11
HEMBA1005403.	CDNA FLJ20062 FIS, CLONE	COL01508.			PFAM: WD domain, G-beta repeat	DJ703H14.1 PROTEIN	(FRAGMENT).		(AK011059) putative [Mus	musculus]				PROTEIN ZERO RELATED PROTEIN.	PFAM: Cytochrome c oxidase subunit III	CYTOCHROME C OXIDASE	POLYPEPTIDE III (EC 1.9.3.1).	CDNA FL/20080 FIS, CLONE COL03184.	CDNA: FLJ21463 fis, clone COL04765.	HYPOTHETICAL PROTEIN	(FRAGMENT).						CDNA: FLJ23235 fis, clone CAS04980.	(AT 136942) himothatical
	blastx.2				HMMER 2.1.1	blastx.2			WUblastx.6	4				blastx.2	HMMER 2.1.1	blastx.2		blastx.2	blastx.2	blastx.2				-			blastx.2	hlacty 2
	20				53				54					99	85			59	09	63							4	29
	837309				815649				813588					847030	866159			853358	561935	695704							637521	866160
	HBJAB02				HBJCR46				HBJDS79					HBJEL16	HBJIG20			HBJKD16	HBMBM96	HBMTX26							HBMTY48	HRMIH74

586	863	863	863	851	863	836	863	851	851	863	863	845	824	836	851	854	851	854	845	863	854	827	842	845	875	836	848	851	851	851	857	821	821	863	851	848
302	585	585	579	585	588	576	576	585	585	585	585	594	826	594	588	594	579	585	579	588	625	585	591	573	585	585	594	579	579	579	288	579	009	929	591	579
92%	72%	%19	64%	61%	%09	47%	42%	43%	46%	44%	43%	47%	46%	46%	43%	45%	42%	44%	42%	42%	41%	42%	42%	40%	41%	41%	40%	39%	43%	43%	40%	45%	44%	37%	42%	41%
gb AAK01205.1																																				
(AF319977) mage-d3 [Mus	musculus]																																			
blastx.2																																				
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990877																																				
HBMWE61																																				

863	845	854	842	815	845	854	851	740	854	842	827	815	842	851	863	851	481	222	204	412	809	069	547	734	831	527	37	74	785	775		1588	1260
585	588	594	579	591	594	585	588	579	579	594	585	579	594	819	579	642	221	1	323	2	1009	836	738	925	668	1051	292	157	964	77		∞ ∞	694
37%	41%	40%	41%	44%	39%	43%	39%	20%	37%	42%	43%	44%	40%	35%	43%	35%	100%	100%	82%	%86	%19	77%	39%	39%	52%	100%	81%	48%	31%	277.3		90%	70%
																	emb CAC25073.1		sp Q9UQ32 Q9UQ32	emb CAC21463.1	sp BAB15071 BAB15071		sp BAB15056 BAB15056			pir JC7127 JC7127				PF00783		sp Q9UDT9 Q9UDT9	pir S72481 S72481
																	(AX062318) unnamed protein	onstruct]	AD 3 (FRAGMENT).	(AL161656) bA12M19.1.3 (novel protein) [Homo sapiens]	CDNA: FLJ21463 fis, clone	COL04765.	CDNA: FLJ21394 fis, clone	COL03536.		frizzled protein 4 - human				PFAM: Inositol polyphosphate phosphatase family, catalytic	domain	WUGSC:H_DJ412A9.2 PROTEIN (FRAGMENT).	nan
		•	-														blastx.2		blastx.2	blastx.2	blastx.2		blastx.2			blastx.2				HMMER 2.1.1		blastx.2	blastx.2
													•				<i>L</i> 9		69	71	72		73			74				92	-1		77
																	834801		810542	856387	639039		637542			837972				761204			847007
																	HBNAX40		HBQAB79	HBSAK32	HBXCM66		HBXCX15			HCDCY76				HCE1G78			HCE2H52

				transposon MER37		%09	564	758
						77%	430	564
HCE3B04	831151	78	blastx.2	HYPOTHETICAL 31.3 KDA	sp 043466 043466	49%	217	972
				PROTEIN (FRAGMENT).		53%	300	758
						%86	836	1003
						%06	401	490
HCEDR26	771144	80	blastx.2	CDNA FLJ20489 FIS, CLONE KAT08285.	sp Q9NX17 Q9NX17	%69	1417	1115
нсее 25	531784	82	blastx.2	SODIUM CHANNEL 2.	sp P78349 P78349	95%	311	433
						100%	658	714
						93%	433	480
HCEEU18	688041	83	blastx.2	UNNAMED PORTEIN	sp Q9N083 Q9N083	26%	1223	933
				PRODUCT.		46%	186	10
HCEFZ82	831745	84	blastx.2	(BC001698) Similar to lipase	gb AAH01698.1 AAH016	100%	17	604
				protein [Homo sapiens]	86	95%	594	782
HCFLN88	610000	98	blastx.2	BCL7B protein - human	pir S58284 S58284	%98	278	475
HCHAB84	834326	88	blastx.2	(AX061649) unnamed protein product [Homo sapiens]	emb CAC25009.1	2001	82	744
HCNSD29	862314	91	blastx.2	HUNTINGTIN-	sp 075400 075400	%66	337	1605
				INTERACTING PROTEIN HYPA/FBP11 (FRAGMENT).	-			
HCRAY10	602269	96	blastx.2	HSPC244.	sp Q9P0N5 Q9P0N5	40%	192	437
HCRBF72	828945	26	blastx.2	MITOTIC SPINDLE ASSEMBLY CHECKPOINT PROTEIN MAD2B 1	sp Q9UI95 MD22_HUM AN	100%	191	823
HCUCF89	637986	100	blastx.2	PRO2822.	sp Q9P147 Q9P147	84%	503	426
HCUCK44	790277	101	blastx.2	hypothetical protein	pir T34520 T34520	%66	29	529
				DKFZp564J157.1 - human (fragment)				
HCWFU39	651316	104	blastx.2	CDNA FLJ20366 FIS, CLONE HEP18008.	sp Q9NX95 Q9NX95	100%	266	926
HDPDI72	897277	109	blastx.2	adult-specific brush border protein - rabbit	pir C45665 C45665	%19	=	223
HDPD158	587265	110	blastx.2	hypothetical protein DKFZp434D2328.1 - human	pir T42691 T42691	%9L 100%	746	1450
						0/ 001	700	170

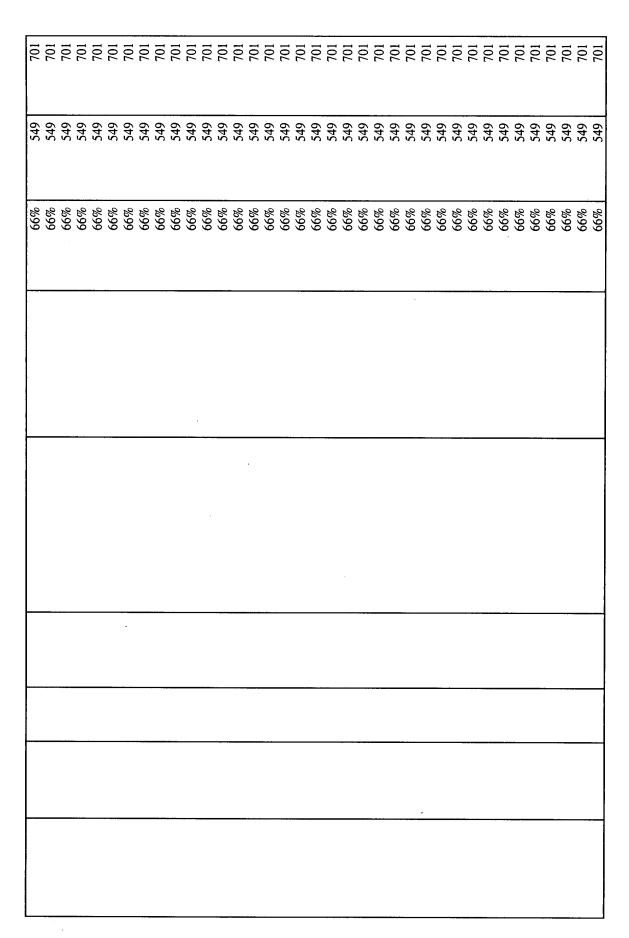
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307	785	1393	1327	627	624	621	1402	624	1447	624	1220	585	307	621	307	618	1402	615	618	313	307	307	286	307	1464	779	316	1042	785	1144	274	307	307	307	594	540
14	621	785	959	307	307	325	848	259	854	259	1137	322	92	319	68	337	905	307	307	101	98	83	92	134	1405	624	68	827	630	848	68	101	131	125	340	307
100%	87%	33%	30%	38%	35%	36%	30%	36%	31%	33%	<i>1</i> %96	37%	37%	30%	37%	31%	26%	29%	33%	36%	32%	35%	35%	37%	100%	41%	34%	40%	40%	26%	35%	36%	33%	37%	32%	33%
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316	1402	624	618	1117	307	179	1402	1411	785	773	307	785	881	316	785	785	785	794	176	172	909	785	785	671	618	1223	1220	1220	1220	1184	800	965	1593	1641	1440
74	803	487	358	962	68	624	1229	1265	099	645	137	099	633	188	654	645	645	624	624	68	454	630	999	543	553	1134	1137	1125	1149	1125	729	285	1153	1306	117/
30%	28%	41%	29%	41%	27%	33%	34%	36%	36%	39%	33%	36%	33%	37%	31%	35%	35%	31%	34%	42%	35%	34%	31%	34%	45%	33%	35%	28%	37%	20%	65.1	38%	42%	32%	01/77
																															PF00560	emb CAA80847.1			
																															PFAM: Leucine Rich Repeat	garp [Homo sapiens]			
																															HMMER 2.1.1	Ublastx.6	4		
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																															853513				
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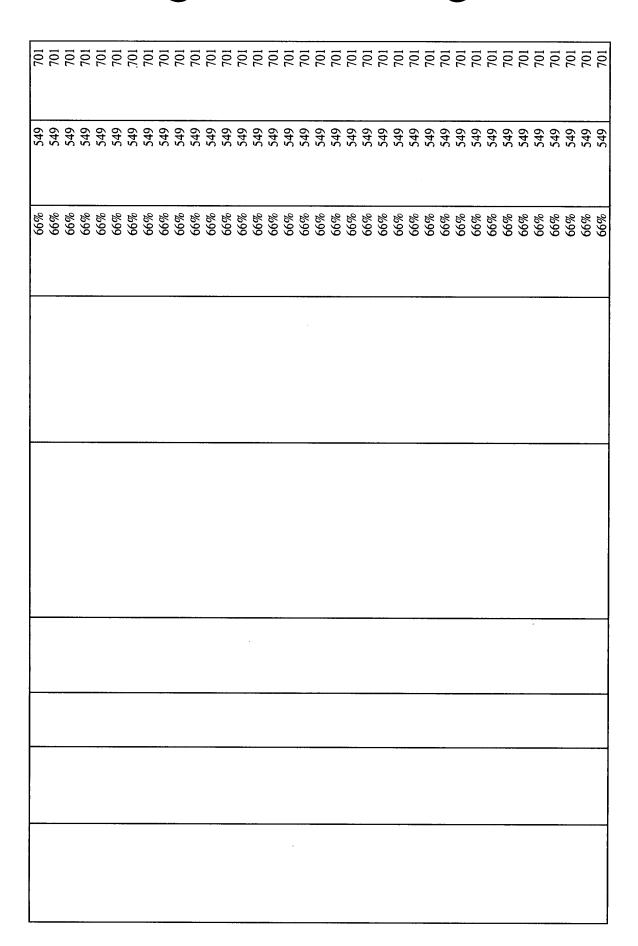
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1614	1159	1174	1306	1174	1162	1183	468	246	1629	327	220	1418	1413	1452	2528	2594	2525	2533	1858	1314	1813	1301	1457	2625	2242	2527	1857	1857	1364	1836	1305	2461	1800	2522	1380
31%	26%	30%	33%	30%	31%	33%	28%	27%	37%	%66	93%	26%	52%	55%	71%	52%	77%	62%	62%	53%	%99	39%	40%	21%	44%	29%	21%	20%	26%	51%	39%	53%	%99	48%	%09
										sp 060704 TPS2_HUMA	Z	sp 060448 060448																							
										PROTEIN-TYROSINE	SULFOTRANSFERASE 2 (EC 2.8.2.20) 1	NEURONAL THREAD	PROTEIN AD7C-NTP.																						
										blastx.2		blastx.2																							
										112		114																							
										790189		801947														٠									
										HDPFU43		HDPGE24																							

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2625	2366	2187	1813	1883	1413	1226	1215	63	2	1313	505	549	549	549	549	549	549	549	549	549	549	249	549	249	549	549	549	549	549	549	549	549	549
45%	31%	47%	20%	20%	%09	26%	28%	%66	%86	44%	40%	%89	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	299	%99	%99	%99	%99	%99	%99
			J					sp BAB14138 BAB14138	sp BAB14615 BAB14615	sp BAB13972 BAB13972		dbj BAA97098.1																					
								CDNA FLJ12564 fis, clone NT2RM4000833.	CDNA FLJ13518 fis, clone PLACE1005799.	CDNA FLJ12089 fis, clone	HEMBB1002550, weakly similar to 1	(AP002460)	gene_id:F1D9.26~unknown	protein [Arabidopsis thaliana]																			
	-							blastx.2	blastx.2	blastx.2		blastx.2																					
								115	116	117		119																					
			,					813352	777493	745377		637588																					
								HDPIU94	HDPOC24	HDPOL37		НДРРД93																					

701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701	701
549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549	549
2699	2699	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	299	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	%99	299	%99
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				 		549 701					969 265	985		092 208	6 155	965 1153			340	13 303	
2 %99	999	 999				999			999		85% 85%	76%		81%	94%	6 %99			% 06	100%	
													sp Q9NX85 Q9NX85		pir S09875 S09875	sp Q9N083 Q9N083	-		pir A00422 DNHUN3	emb CAB66872.1	
													20378 FIS, CLONE	KAIA0536.	hypothetical protein UL126 - human cytomegalovirus (strain AD169)	UNNAMED PORTEIN	PRODUCT.		NADH dehydrogenase (ubiquinone) (EC 1.6.5.3) chain 3 - human mitochondrion		
													blastx.2		blastx.2	blastx.2			blastx.2	blastx.2	
													120		121	123			124	125	
													684292		778405	852328		001000	838139	801898	
													HDPPQ30		HDPPW82	нDQHM36		117.00	HD1AU33	HDTAV54	

1757 1744	1075	1075	1015	1015	1075	1135	449	1300	1378	633 928	490	771	1642	1501	783	206	741	206	1663	1553	1172	1663	1553	1172	1414	1102	1345	613	1267
1347	491	494	491	200	533	638	565	125	938	19 623	ς.	244	782	863	145	782	190	782	1845	1672	1312	1845	1672	1312	2	2	389	7	7 1
81%	%66	44%	47%	47%	42%	29%	%19	%66	%86	80%	%66	184.7	%86	38%	77%	45%	33%	47%	72%	75%	46%	72%	75%	46%	75%	85%	81%	84%	48%
	sp Q9P2S7 Q9P2S7						sp Q9SNH1 Q9SNH1	sp Q9NVC4 Q9NVC4	sp BAB14967 BAB14967	pir A46312 A46312	sp 095476 095476	PF00092	emb CAA07569.1						sp Q9NX85 Q9NX85			sp Q9NX85 Q9NX85			6ILU9Ql9ILU9Qlqs				
	CISPLATIN RESISTANCE-	ASSOCIATED	OVEREXPRESSED	PROTEIN.			SIMILAR TO RING-H2 FINGER PROTEIN RHA1A.	CDNA FLJ10814 FIS, CLONE NT2RP4000984.	CDNA: FLJ21047 fis, clone CAS00253.	gag polyprotein - human endogenous virus S71	HYPOTHETICAL 28.3 KDA PROTEIN.	PFAM: von Willebrand factor type A domain	(AJ007581) matrilin-4 [Homo	sapiens]					CDNA FLJ20378 FIS, CLONE	KAIA0536.		CDNA FLJ20378 FIS, CLONE	KAIA0536.		HYPOTHETICAL 105.9 KDA	PROTEIN.			
	blastx.2						blastx.2	blastx.2	blastx.2	blastx.2	blastx.2	HMMER 2.1.1	WUblastx.6	4					blastx.2			blastx.2			blastx.2				
	130						132	133	136	137	138	139							141			142			145			•	
	888705						553651	753265	762960	562767	847058	827236							843781			845672			856544				
	HE2CA60						НЕ2СМ39	HE2HC60	HE6CS65	HE6D092	HE6EY13	НЕ6FU11							HE8FC45			HE8FC45			HE8FD92				

1102	1075	1345	331	609	240	462	297	297	270	462	540	240	540	540	258	480	411	408	408	411	411	411	411	141	168	129	1696	1868	938	1891	1840	789	1110	1022	1720
167	47	605	101	4	4	1	-		31	4	331	331	331	316	40	25	25	61	19	202	202	202	187	25	25	58	1860	2020	318	761	878	736	1304	1111	1863
48%	41%	39%	38%	95%	83%	45%	57%	26%	929	40%	62%	62%	%09	20%	43%	94%	78%	48%	48%	62%	62%	%09	20%	28%	43%	41%	%69	299	94%	%66	28%	55%	81%	80%	81%
				eILU6O eILU6O ds												91109091119											sp BAB15071 BAB15071		sp[Q9JIH1 Q9JIH1	pir S14458 S14458			sp Q9NX85 Q9NX85		sp Q9NX85 Q9NX85
				HYPOTHETICAL 105.9 KDA	PROTEIN.											HYPOTHETICAL 105.9 KDA	PROTEIN.										CDNA: FLJ21463 fis, clone	COL04765.	ZINC FINGER PROTEIN 289.	laminin alpha-1 chain precursor	- human		CDNA FLJ20378 FIS, CLONE	KAIA0536.	CDNA FLJ20378 FIS, CLONE KAIA0536.
				blastx.2												blastx.2											blastx.2		blastx.2	blastx.2			blastx.2		blastx.2
				146												147											148		149	151			157		158
				869847												901142											862016		899528	962178			847064		798096
				HE8FD92												HE8FD92											HE8SG96		HE8TY46	HE9EA10			HEBFR46		HEBGE07

COSSIDSE COLECL

2110 1802 2111 2079	1255 1031	509 838	85 426	423 515	30	1107 805				855 826	856 827	3 356	324 1058	438 581		1071 1178			1083 1172	-		486 584	662 809	263 403		908 688	13 399		241 1722
%06 %69	29%	63%	92%	83%	81%	58%	%19	20%	20%	20%	%0 <i>L</i>	%66	100%	%68	87%	44%	34%	29%	30%	%6L	83%	39%	21%	91%	26%	46%	100%		%58 ~~~~
sp BAB15071 BAB15071	sp BAB15071 BAB15071	sp AAG35515 AAG35515	pir A01852 CSBOAB			sp BAB15071 BAB15071	splQ9NX85 Q9NX85					sp Q9P0V3 Q9P0V3	gb AAG44596.1 AF25129 6_1	sp Q14152 IF3A_HUMA	Z					sp Q9Z320 Q9Z320				pir S44279 S44279	sp Q9UHT1 Q9UHT1		sp Q9UHE8 STEA_HUM	Alv	pir T18526 T18526
CDNA: FLJ21463 fis, clone COL04765.	CDNA: FLJ21463 fis, clone COL04765.	PRO2550.	peptidylprolyl isomerase (EC	5.2.1.8) A - bovine		CDNA: FLJ21463 fis, clone COL04765.	CDNA FLJ20378 FIS, CLONE	KAIA0536.				BOG25.	(AF251296) TPA018 [Homo sapiens]	EUKARYOTIC	TRANSLATION INITIATION	FACTOR 3 SUBUNIT 10 1				C29.				CDM protein - human	PRO1902 PROTEIN.		SIX TRANSMEMBRANE	EFITHELIAL ANTIGEN OF PROSTATE.	SREBP cleavage activating
blastx.2	blastx.2	blastx.2	blastx.2			blastx.2	blastx.2					blastx.2	blastx.2	blastx.2						blastx.2				blastx.2	blastx.2		blastx.2		blastx.2
160	161	164	166			167	168					169	170	175						176				177	179		180		181
693175	637624	834491	855935			701984	786205		-			844543	790557	701985						98889				580824	839206		847074		827572
HELAT35	HELBU54	HEMEY47	HEPBA14			нЕQАН80	HEQBF89					HETCI16	HETDW58	HFCFE20						HFEAY59				HFGAJ16	HFIJA29		HFIJA68		HFKES05

HFKEU12	634006	182	blastx.2	hypothetical protein 3 - rat	pir S21347 S21347	62%	387	692
						38%	756	1031
						51%	757	933
						53%	569	778
HFPDS07	821646	185	blastx.2	(AF327434) glutaminase	gb AAG47842.1 AF32743	84%	2	436
				[Homo sapiens]	4_1	266	343	528
HFVGK35	731868	189	blastx.2	CDNA: FLJ21463 fis, clone COL04765.	sp[BAB15071]BAB15071	%09	528	833
HFVHW43	570948	190	blastx.2	CDNA FLJ11786 fis, clone HEMBA1006036.	sp BAB13911 BAB13911	%19	1223	1068
HFXAV37	626595	191	blastx.2	NEURONAL THREAD	sp O60448 O60448	29%	1453	1187
				PROTEIN AD7C-NTP.		64%	209	407
						%69	909	406
						52%	1472	1218
						%69	209	461
						28%	1454	1275
						%89	473	333
						26%	1295	1173
						37%	558	346
						45%	1342	1232
						43%	1408	6911
						47%	1366	1232
						42%	1412	1275
						78%	402	361
						%09	1240	1166
						31%	249	355
						75%	1404	1357
						43%	1454	1386
						40%	1467	1402
						26%	1287	1222
						52%	1229	1179
						47%	209	539
						34%	583	461
						%09	368	354
						46%	1187	1110
HFXBT66	580831	193	blastx.2	CDNA: FLJ21463 fis, clone	sp BAB15071 BAB15071	63%	535	208
				COL04765.		54%	808	913

1063	52	491	5	2712	1473	1473	1471	1495	1495	1495	1525	1540	1615	1648	1401	707	924	715	167	470	145	1872	2407	1818	1787	2461	2348	1829	2530	2392	2348	2416
1284	537	541	94	361	184	1057	182	890	1049	866	1052	1052	926	1052	1949	991	465	611	129	420	90	2597	2631	2048	2029	2631	2464	1963	2631	2541	2410	2475
72%	45%	52%	30%	100%	%66	38%	%66	53%	64%	53%	52%	48%	34%	36%	%66	2008	81%	91%	92%	64%	100%	43%	71%	%99	63%	63%	28%	20%	44%	41%	%99	%09
sp Q9NX17 Q9NX17	sp 000372 000372			sp Q9UIE9 Q9UIE9	sp BAB15362 BAB15362		sp BAB15362 BAB15362								sp Q9NPB0 Q9NPB0	spi001141 0011141					pir A49465 A49465	sp O60448 O60448										
CDNA FLJ20489 FIS, CLONE KAT08285.	PUTATIVE P150.			WUGSC:H_DJ0687K01.2 PROTEIN.	CDNA: FLJ22454 fis, clone	HRC09703 (Fragment).	CDNA: FLJ22454 fis, clone	HRC09703 (Fragment).							DJ202I21.1 (NOVEL PROTEIN) (CDNA FLJ11101 FIS CY ONE 1	PARS GDP/GTP EXCHANGE	FACTOR HOMOLOGUE.				coatomer zeta chain - bovine	NEURONAL THREAD	PROTEIN AD7C-NTP.									
blastx.2	blastx.2			blastx.2	blastx.2		blastx.2								blastx.2	hlacty 2	7				blastx.2	blastx.2										
195	198			199	200		201								202	204	2				205	206										
826710	693011			851527	801999		842540								765278	886174					778071	753230										
HGBER72	HGBHP91			HGCAC19	HGCAC19	•	HGCAC19								HHEAK45	HHEOW19	}				HHFFF87	HHFFL34										

1780	2345	2348	1993	251	499	503	496	1290	1324 407	7176	159	1169	1171	1447	767	964	471	602	475	896	390	1004	969
1884	2401	2410	2043	3	295	574	292	1580	479 270	1273	103	168	104	788	198	464	199	396	14	414	395 370	348	6
42%	52%	%99	52%	100%	%56	91%	95%	%69	99%	72%	73%	100%	%66	100%	%86	52%	57%	52%	100%	82%	100%	49%	%001
				sp CAC13124 CAC13124	sp Q9SNH1 Q9SNH1			sp BAB15071 BAB15071	sp BAB15499 BAB15499	sp BAB15071 BAB15071	dbj BAA92023.1		sp O9NUU6 O9NUU6	sp Q9UH94 Q9UH94		sp O45030 O45030		sp BAB14376 BAB14376	pir JC7110 JC7110	gb AAG44724.1 AF26785	5_1	sp Q9VWB1 Q9VWB1	sp 095235 RB6K_HUMA N
				Golgi protein.	SIMILAR TO RING-H2	FINGER PROTEIN RHA1A.		CDNA: FLJ21463 fis, clone COL04765.	CDNA: FLJ22888 fis, clone KAT03934.	CDNA: FLJ21463 fis, clone COL04765.	(AK001989) unnamed protein	product [Homo sapiens]	CDNA FLJ11127 FIS, CLONE PLACE1006225.	PROLACTIN REGULATORY	ELEMENT-BINDING PROTEIN (PROLACTIN REGULATORY BINDING- ET FMENT PROTFIN)	STRABISMUS.		CDNA FLJ12988 fis, clone NT2RP3000080.	brain-specific membrane anchor protein - human	55) HT034 [Homo	sapiens]	CG6597 PROTEIN.	RABKINESIN-6 (RAB6- INTERACTING KINESIN- LIKE PROTEIN) 1
				blastx.2	blastx.2			blastx.2	blastx.2	blastx.2	WUblastx.6	4	blastx.2	blastx.2		blastx.2		blastx.2	blastx.2	blastx.2		blastx.2	blastx.2
				202	208			509	213	214	217		218	516		220		221	222	223		224	526
				824059	634605			658692	801910	862028	782450		958698	843549		638329		824062	862029	793678		801960	840365
				HHFFS40	HHGCS78			HHGDT26	HHSB165	HHSDI53	HILCA24		HILCA24	HISAT67		HJBCU75		HJMAA03	HJMAV41	HJMAY90		HJPBE39	НЈРСН08

95 1582	886 1104	1753 1400	1995 1630	856 701 1008 832		714 797		693 797	105 1142	8111 118	2 469	1833 1585	1837 1811			1831 1808	1098 1412	32 547	3 584	10 90	935 807		
9,										2	92							9.	9.	9.			
42%	72%	93%	64%	65%	926	92%	%08	77%	%06	%66	%66	72%	88%	25%	879	82%	45%	%16	.100%	%001	72%	100%	
sp Q9VKC8 Q9VKC8	dbj BAB21923.1	sp Q9P1G7 Q9P1G7	sp Q9NX17 Q9NX17	sp Q9N083 Q9N083	sp BAB15513 BAB15513	-			gb AAC26658.1	sp 075477 075477	sp AAG33617 AAG33617	sp Q9NX17 Q9NX17					859790 859790 ds	gb AAG48521.1	pir A90470 FGHUG	sp Q9P2Y2 Q9P2Y2	sp BAB12374 BAB12374	sp P78380 P78380	
CG6756 PROTEIN.	(AB055298) hypothetical protein [Macaca fascicularis]	PRO1777.	CDNA FLJ20489 FIS, CLONE KAT08285.	UNNAMED PORTEIN PRODUCT.	CDNA: FLJ22976 fis, clone	KAT11222 (Fragment).	· ·		(AF064093) KE04p [Homo sapiens]	KE04P.	ATP-binding cassette half- transporter.	CDNA FLJ20489 FIS, CLONE	KAT08285.				LINE-1 ELEMENT ORF2.	(AF140225) unknown [Homo sapiens]	fibrinogen gamma-A chain precursor [validated] - human	BETA-1,4 MANNOSYLTRANSFERASE	Hypothetical 9.0 kDa protein.	LECTIN-LIKE OXIDIZED LDL RECEPTOR.	
blastx.2	blastx.2	blastx.2	blastx.2	blastx.2	blastx.2				WUblastx.6	blastx.2	blastx.2	blastx.2					blastx.2	blastx.2	blastx.2	blastx.2	blastx.2	blastx.2	
227	228	229	230	232	234				237	512	238	239		·			240	241	242	245	246	249	
838573	853361	790192	738797	734213	695732				740755	837599	830544	638476					560663	883431	840321	701996	647603	886180	
HKABU43	HKACI79	HKAFF50	HKGBF25	HKMLK03	HKTAB41				нг.ролу	HLDQU79	HLDRT09	HLHAP05					HLHCS23	HLIBO72	HLICE88	HLMBW89	HLMGP50	HLQAS12	

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548	1216	657 872	518	391	1455	1455	1455	1456	1055	068	2206	1159	757	1135	794	391	892	3
18	1100	1 660	204	221	106	106	106	107	6	1186	2	104	101	794 2629	81	137	8 269	182
%86	87%	98%	%16	94%	100%	100%	100%	100%	100%	72%	%66	46%	38%	40%	100%	100%	99%	85%
pir JC5973 JC5973	65IU6Q 62IU6Q qs	sp BAB14955 BAB14955	emb CAB66638.1	sp BAB14578 BAB14578	gb AAD41160.1 AF04228 4_1	sp Q9Y6N5 Q9Y6N5	sp Q9Y6N5 Q9Y6N5	sp Q9Y6N5 Q9Y6N5	8MQU6QM8 Q9UQM8	sp Q9NX17 Q9NX17	sp Q9NSE4 Q9NSE4	sp Q9VYV3 Q9VYV3			sp AAG23165 AAG23165	sp Q9NVW5 Q9NVW5	sp AAG18444 AAG18444	sp BAB15511 BAB15511
aquaporin 9 - human	PRO0478 PROTEIN.	CDNA: FLJ21016 fis, clone CAE05735.	(AL136703) hypothetical protein [Homo sapiens]	CDNA FLJ13386 fis, clone PLACE1001104, weakly similar to 1	(AF042284) unknown [Homo sapiens]	HYPOTHETICAL 50.0 KDA PROTEIN.	HYPOTHETICAL 50.0 KDA PROTEIN.	HYPOTHETICAL 50.0 KDA PROTEIN.	CGI-44 PROTEIN.	CDNA FLJ20489 FIS, CLONE KAT08285.	MITOCHONDRIAL ISOLEUCINE TRNA SYNTHETASE (FRAGMENT).	CG1837 PROTEIN.			Rab3 interacting protein variant 4 (Fragment).	CDNA FLJ10468 FIS, CLONE NT2RP2000007.	Guanine nucleotide binding protein beta subunit 5L.	CDNA: FLJ22969 fis, clone
blastx.2	blastx.2	blastx.2	blastx.2	blastx.2	WUblastx.6	blastx.2	blastx.2	blastx.2	blastx.2	blastx.2	blastx.2	blastx.2			blastx.2	blastx.2	blastx.2	blastx.2
	251	258	261	263	264	265	266	267	268	270	272	273			274	275	279	281
	584786	838453	838083	658703	839783	858210	867910	887445	668249	584789	783077	837027			840077	587307	847403	709672
	HLQCX36	HLWDB73	HLYGB19	HLYGY91	HMCAZ04	HMCAZ04	HMCAZ04	HMCAZ04	HMCAZ04	HMDAB29	HMEBB82	HMEDE24			HIMEDI90	HMELM75	HMICP65	HMSBE04

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HMSCL38	801919	282	blastx.2	CDNA: FLJ21463 fis, clone	sp BAB15071 BAB15071	55%	1155	1472
-				COL04765.		71%	2841	2653
						74%	2935	2855
HMSCR69	843059	283	HMMER 2.1.1	PFAM: Zinc finger present in dystrophin, CBP/p300	PF00569	48.2	113	250
			blastx.2	POTASSIUM CHANNEL MODULATORY FACTOR.	sp Q9P0J7 Q9P0J7	%66	107	1249
HMSHC86	840402	284	blastx.2	UNNAMED PORTEIN	sp Q9N083 Q9N083	%19	1674	1420
				PRODUCT.		54%	1398	1234
						. 70%	1724	1674
HMSHU20	847410	285	WUblastx.6	(AK025116) unnamed protein product [Homo sapiens]	dbj BAB15071.1	47%	1722	1453
HMTAB77	847411	287	blastx.2	matrin 3 - rat	pir A40016 A40016	87%	1024	2520
						100%	920	1055
						%86	242	628
						53%	2311	2760
	:					%86	3258	3428
						26%	2584	2763
						31%	2596	2709
						35%	1705	1797
						35%	3312	3404
HMUAE26	747403	288	blastx.2	SEVEN TRANSMEMBRANE	sp Q9P2R4 Q9P2R4	%66	577	1272
				DOMAIN ORPHAN RECEPTOR.		100%	153	575
HMUAN45	833072	289	blastx.2	UNNAMED PORTEIN	sp Q9N092 Q9N092	61%	239	1516
				PRODUCT.		2002	684	1238
						36%	346	1080
						30%	2022	2231
HMVBC31	825598	290	blastx.2	PRENYLCYSTEINE	sp 060725 060725	100%	88	682
				CARBOXYL METHYLTRANSFERASE.		80%	747	938
HMVDU15	801969	291	blastx.2	CGI-30 PROTEIN.	sp Q9Y319 Q9Y319	94%	75	917
HMWBL03	822861	292	blastx.2	hypothetical protein DKFZp762L0311.1 - human	pir T50635 T50635	26%	617	1237
				(fragment)				
HMWJF53	758158	293	blastx.2	Nuclear LIM interactor-	sp AAG15402 AAG15402	100%	154	720
				וווכומרחוון ומרוטו.		91%	3	1/0

799541 295 815675 297 815676 298	blastx.2		PRUDUCI.			•	
		tx.2	HT015 PROTEIN.	sp Q9NYZ2 Q9NYZ2	100%	1756	2202
	İ				26%	1762	2289
	blastx.2	tx.2	(AB055283) hypothetical	dbj BAB21907.1	43%	1667	1825
			protein [Macaca fascicularis]		64%	58	66
					21%	6	20
					40%	53	247
					44%	6	95
					53%	59	97
	blastx.2 	tx.2	(AF308287) serologically defined breast cancer antigen NY-BR-20 [Homo sapiens]	gb AAG48255.1 AF30828 7_1	100%	425	282
722237 300	blastx.2	tx.2	(AF205218) NS1-binding	gb AAG43485.1	100%	6	431
	•		protein-like protein [Homo		34%	6	404
			sapiens]		35%	3	407
					33%	6	407
					32%	129	422
603910 301	blastx.2	tx.2	NEURONAL THREAD	sp 060448 060448	74%	714	914
			PROTEIN AD7C-NTP.		%99	702	878
					%19	733	915
					45%	631	903
					25%	530	631
					43%	542	402
					62%	629	715
					62%	979	902
ı	1				37%	527	751
688114 302	blastx.2	tx.2	CDNA: FLJ21463 fis, clone	sp BAB15071 BAB15071	%59	818	1018
			COL04765.		85%	1081	1143
	1				73%	1020	1076
597449 310	blastx.2	tx.2	Hypothetical 14.1 kDa protein.	sp BAB12154 BAB12154	47%	398	541
					32%	69	302
852178 313	blastx.2	IX.2	probable oxysterol-binding protein DJ430N08.1 - human (fragment)	pir T02435 T02435	200%	128	6
834487 320	blastx.2	x.2	hypothetical protein	pir T47135 T47135	929	822	583

	485	10	37	177	248	1691	902	561	594	711	14	286	14	653	2	286	794	54	1440	1342	947	099	704	199	331	1916	109	159	529	792	510
	733	483	483	236	337	894	888	854	719	887	100	885	106	718	130	639	898	80	556	743	729	589	183	999	8	132	14	106	29	529	172
	48%	37%	33%	25%	36%	64%	62%	20%	%99	40%	63%	33%	26%	%89	30%	25%	38%	77%	26%	43%	78%	41%	%66	100%	%98	%86	100%	88%	%88	%06	44%
	sp P11369 POL2_MOUS	田				sp 060448 060448													sp Q9UK58 Q9UK58				sp BAB14854 BAB14854	sp Q13878 Q13878	sp Q9NSI6 WDR9_HUM AN	sp BAB14427 BAB14427			sp Q9NXS2 Q9NXS2		88XN6O 88XN6O as
DKFZp761L0812.1 - human (fragment)	RETROVIRUS-RELATED	POL POLYPROTEIN	[CONTAINS: REVERSE	TRANSCRIPTASE (EC	2.7.7.49); ENDONUCLEASE].	NEURONAL THREAD	PROTEIN AD7C-NTP.												CYCLIN L ANIA-6A.				CDNA FLJ14158 fis, clone NT2RM1001112.	94 KDA B-RAF PROTEIN (FRAGMENT).	WD-REPEAT PROTEIN 9 (FRAGMENT).	CDNA FLJ13081 fis, clone	NT2RP3002033.		CDNA FLJ20084 FIS, CLONE	COL03526.	CDNA FLJ20374 FIS. CLONE
	blastx.2					blastx.2								·					blastx.2				blastx.2	blastx.2	blastx.2	blastx.2			blastx.2		blastx.2
	321					322													324				328	331	332	333			334		335
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								PHOSPHATIDYLINOSITOL GLYCAN, CLASS L (EC 3.5	CDNA FLJ11238 FIS, CLONE PLACE1008532.	(AB055293) hypothetical	protein [Macaca fascicularis]			(AF261138) HT032 [Homo sapiens]	PRO2822.	Hypothetical 17.2 kDa protein.	Angiopoietin-like protein PP1158.	ribosomal protein L15, cytosolic [validated] - rat	CG12001 PROTEIN.	WUGSC:H_DJ0593H12.2 PROTEIN.	(AL136914) hypothetical	NAG13.				\neg	CDNA ET 120AAS ETC OT ONE
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								HORBV76	HOSDO75	HOSEC25				HOSEJ94	HOUCA21	HOUDE92	HOUDR07	HOUED72	HOUFS04	ноин125	HPCAL26	HPFBA54					HPFCI36

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562779 363 blastx.2 612870 364 blastx.2 843592 366 blastx.2 845752 367 blastx.2 695752 370 blastx.2 853551 372 blastx.2 812879 373 blastx.2 866187 376 blastx.2 866481 378 blastx.2		sp Q9P1E1 Q9P1E1	24%	187	44
843592 366 blastx.2 845752 367 blastx.2 695752 370 blastx.2 824074 371 blastx.2 853551 372 blastx.2 812879 373 blastx.2 827302 377 blastx.2 866481 378 blastx.2	blastx.2	sp AAG35515 AAG35515	%59	646	467
843592 366 blastx.2 845752 367 blastx.2 695752 370 blastx.2 824074 371 blastx.2 853551 372 blastx.2 812879 373 blastx.2 827302 377 blastx.2 866481 378 blastx.2			26%	786	613
843592 366 blastx.2 845752 367 blastx.2 695752 370 blastx.2 824074 371 blastx.2 853551 372 blastx.2 812879 373 blastx.2 827302 377 blastx.2 866481 378 blastx.2	blastx.2	sp Q99770 Q99770	%59	614	384
843592 366 blastx.2 845752 367 blastx.2 695752 370 blastx.2 824074 371 blastx.2 853551 372 blastx.2 866187 376 blastx.2 827302 377 blastx.2			26%	384	334
845752 367 blastx.2 695752 370 blastx.2 824074 371 blastx.2 853551 372 blastx.2 866187 376 blastx.2 866481 378 blastx.2	blastx.2	sp Q9NX85 Q9NX85	26%	885	209
845752 367 blastx.2 695752 370 blastx.2 824074 371 blastx.2 853551 372 blastx.2 866187 376 blastx.2 866481 378 blastx.2		ᅱ	28%	605	513
695752 370 blastx.2 824074 371 blastx.2 853551 372 blastx.2 866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2	blastx.2	sp Q9NX85 Q9NX85	54%	891	209
824074 371 blastx.2 853551 372 blastx.2 812879 373 blastx.2 866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2			28%	909	513
853551 372 blastx.2 853551 372 blastx.2 812879 373 blastx.2 866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2		sp BAB17282 BAB17282	%16	534	116
824074 371 blastx.2 853551 372 blastx.2 812879 373 blastx.2 866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2			989	2	919
824074 371 blastx.2 853551 372 blastx.2 812879 373 blastx.2 866187 376 blastx.2 866481 378 blastx.2			64%	214	549
824074 371 blastx.2 853551 372 blastx.2 812879 373 blastx.2 866187 376 blastx.2 866481 378 blastx.2			29%	935	1015
853551 372 blastx.2 812879 373 blastx.2 866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2	blastx.2	sp Q9Y2A7 NCP1_HUM	100%	1021	1926
853551 372 blastx.2 812879 373 blastx.2 866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2	PROTEIN I (NAP 1)	AN	91%	387	1019
853551 372 blastx.2 812879 373 blastx.2 866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2			94%	11	481
812879 373 blastx.2 866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2	blastx.2	pir T50629 T50629	%86	296	613
812879 373 blastx.2 866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2	DKFZp762L1710.1 - human		100%	2	250
812879 373 blastx.2 866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2					
866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2	blastx.2	sp Q9UJU6 Q9UJU6	%66	86	940
866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2	DOMAIN-CONTAINING		35%	2	448
866187 376 blastx.2 827302 377 blastx.2 866481 378 blastx.2	PROTEIN HIP-55 (DREBKIN F).				
866481 378 blastx.2	blastx.2	sp BAB15151 BAB15151	%66	23	1393
866481 378 blastx.2	blastx.2	pir T32961 T32961	74%	899	931
866481 378 blastx.2			48%	387	899
000620	blastx.2	sp BAB15246 BAB15246	2686	13	825
000000	HRC00632.		%86	813	1379
800628 370 1-15-4 3			77%	1291	1593
1 800638 1 370 1 15.0001			34%	1590	1685
3 600026 379 DIASTX.2	blastx.2	sp AAG17847 AAG17847	%66	47	1174
560720 381 blastx.2	blastx.2	sp BAB15071 BAB15071	70%	1495	1334
HRDDQ39 840405 382 blastx.2 CDNA FLJ20378	blastx.2	splQ9NX85 Q9NX85	%99	775	578

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				KAIA0536.		53%	582	436
HRDER22	9\$0889	383	blastx.2	CDNA FLJ10390 FIS, CLONE	70WN60 C0WN60 ds	100%	6	443
				NT2RM4000104, MODERATELY SIMILAR TO	· .	41%	63	347
HRDEX93	816046	384	blastx.2	PEFLIN.	sp Q9UBV8 Q9UBV8	100%	13	864
HRDFK37	840381	385	blastx.2	UNNAMED PROTEIN PRODUCT.	sp Q9N032 Q9N032	27%	487	642
HRGBD54	828436	386	blastx.2	HPK/GCK-LIKE KINASE	gp 095819 095819	78%	379	2019
				HGK.	•	%69	253	831
						81%	32	253
						27%	9	149
HSAVA08	280870	388	blastx.2	(AB055293) hypothetical	dbj BAB21918.1	%99	1059	934
				protein [Macaca fascicularis]		46%	941	792
						57%	949	968
	,					.63%	962	764
HSAVW42	637660	389	blastx.2	SIMILAR TO RING-H2	sp Q9SNH1 Q9SNH1	81%	595	497
				FINGER PROTEIN RHAIA.		73%	594	493
HSAWZ40	634000	391	blastx.2	ORF2-LIKE PROTEIN (FRAGMENT)	sp 000549 000549	64%	613	8
HOD ZAKEA	020203	200	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	MANUAL 1		2/15	7.71	010
5L/Z4V1.34	0/8/60		Diastx.2	NALDH denydrogenase (ubiquinone) (EC 1.6.5.3) chain 3 - human mitochondrion	pir A00422 DNHUN3	%98 ************************************	226	516
HSHBF76	715838	394	blastx.2	(AF194407) unknown [Homo	gb AAG42221.1	%99	1267	836
				sapiens]		20%	762	460
						72%	834	748
HSJBY32	702020	396	blastx.2	(AJ278118) neuronal nicotinic	emb CAC20435.1	%96	215	514
				acetylcholine alpha 10 subunit [Homo sapiens]		84%	466	684
HSKDR27	580874	397	blastx.2	HYDROXYPROLINE-RICH	9986EQ 9986EQ ds	33%	98	352
				GLYCOPROTEIN (FRAGMENT).		75%	999	691
HSLHX15	777861	399	blastx.2	(AY012159) virion-associated	gb AAG42155.1	100%	180	263
				nuclear-shuttling protein [Mus musculus]		28%	487	522
HSNBM34	635131	402	blastx.2	acyl-CoA dehydrogenase (EC	pir S54183 S54183	2666	113	1546
				1.3.99) very-long-chain		100%	1548	1979

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				specific - human		2507	6300	0110
HSOAHIK	920709	402	1 100ty J	TONIA TI 100480 TIS OI ONT	E 1781 40 O E 1781 40 O	33.70	2022	21/0
	050/20	5	Olastx.2	CDINA FLIZO489 FIS, CLOINE	splosinal/losinal/	25%	707	399
				KA108285.		16%	715	229
						%08	721	692
HSQDO85	853393	405	blastx.2	CG10161 PROTEIN.	sp Q9VCK0 Q9VCK0	64%	485	1021
		-				61%	09	521
						26%	10	57
HSQES57	831222	406	WUblastx.6	(AF151850) CGI-92 protein [Homo sapiens]	gb AAD34087.1 AF15185 0 1	93%	195	086
HSRBE06	871264	407	blastx.2	PRO2550.	sp AAG35515 AAG35515	2002	1626	1327
HSSDI26	560722	408	blastx.2	HYPOTHETICAL 15.4 KDA PROTEIN.	sp Q99770 Q99770	%99	1398	1264
HSSEA64	853395	409	blastx.2	Hypothetical 17.2 kDa protein.	sp AAG17210 AAG17210	%86	7	243
HSSEF77	658725	410	blastx.2	WW DOMAIN BINDING PROTEIN-1.	sp 095637 095637	100%	296	829
HSSFE38	742512	411	HMMER	PFAM: Ribonuclease HII	PF01351	76.3	184	-142
			2.1.1					
			blastx.2	RIBONUCLEASE HI LARGE	sp 075792 RNHL_HUM	%66	587	1051
				SUBUNIT (EC 3.1.26)	AN	%16	156	635
				(RNASE HI 1				
HSWBE76	751308	413	blastx.2	CDNA FLJ10375 FIS, CLONE NT2RM2001950.	sp Q9NW15 Q9NW15	100%	84	266
HSXCP38	895392	414	blastx.2	hydroxymethylglutaryl-CoA lyase (EC 4.1.3.4) - chicken	pir B45470 B45470	73%	17	895
HSYBI06	740766	415	blastx.2	(AB055298) hypothetical	dbj BAB21923.1	78%	821	913
				protein [Macaca fascicularis]		%69	916	954
HT4FV41	853400	418	blastx.2	collagen alpha 1(I) chain - chicken (tentative sequence) 1	pir A90458 CGCH1S	30%	1388	30
HT5GR59	801930	420	blastx.2	DOCKING PROTEIN.	sp 060496 060496	73%	70	1284
1177 4 7770	707707	į				100%	687	1031
HIAEI/8	63/684	421	blastx.2	EMDC II PROTEIN.	sp Q9Y3S0 Q9Y3S0	%06	85	174
HIDAA/8	1 566861	422	blastx.2	(AL137800) dJ127C7.3 (actin	emb CAC19687.1	28%	84	302
				related protein 2/3 complex,				
				subunit 5 (16 kD)) [Homo sapiens]				
HTEAG62	812332	423	blastx.2	HOST CELL FACTOR 2.	sp Q9Y5Z7 Q9Y5Z7	%86	14	2011

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HTLEM16	779133	450	blastx.2	WW DOMAIN BINDING PROTEIN-2.	sp 095638 095638	%66	50	841
HTLFA13	535937	452	blastx.2	CDNA FL/20489 FIS, CLONE KAT08285.	sp[Q9NX17]Q9NX17	26%	1159	839
HTLGI89	835069	454	blastx.2	AP47 protein - mouse	pir S19693 S19693	%86 %86	675	1370
HTLIF11	843506	455	blastx.2	ORNITHINE DECARROXYI ASE.2	sp Q918S4 Q918S4	%65	353	1687
HTLIF12	834946	456	blastx.2	proline-rich protein PRB1/2S (EA) - human (fragment)	pir D40750 D40750	52%	768	323
HTLIF12	842691	457	blastx.2	proline-rich protein PRB1/2S (EA) - human (fragment)	pir D40750 D40750	52%	770	868
HTLIF12	870167	458	blastx.2	proline-rich protein PRB 1/2S (EA) - human (fragment)	pir D40750 D40750	52%	770	868
HTLIF12	886780	459	blastx.2	proline-rich protein PRB1/2S (EA) - human (fragment)	pir D40750 D40750	52%	770	868
HTLIF12	891533	460	blastx.2	proline-rich protein PRB 1/2S (EA) - human (fragment)	pir D40750 D40750	52% 35%	770	868
HTLIF12	901225	461	blastx.2	proline-rich protein PRB1/2S (EA) - human (fragment)	pir D40750 D40750	52% 35%	770	868
HTNBK13	831967	463	blastx.2	(AL136686) hypothetical protein [Homo sapiens]	emb CAB66621.1	100%	123	200
HTOAI50	638623	464	blastx.2	PRO1438.	sp Q9P1H3 Q9P1H3	%89	1251	1138
HTOAM11	664508	465	blastx.2	CDNA: FLJ21463 fis, clone COL04765.	sp BAB15071 BAB15071	75%	603	433
HTOEV16	853616	468	blastx.2	1-ACYL-SN-GLYCEROL-3- PHOSPHATE ACYLTRANSFERASE DELTA (EC 1 1 1	sp Q9NRZ5 PLCD_HUM AN	%86 %66	379 201	1164
HTOH021	732808	470	blastx.2	P47 LBC oncogene - human	pir 138434 138434	%16	581	438
нтонооз	853621	471	blastx.2	CYCLIN-E BINDING PROTEIN 1.	sp Q9UII4 Q9UII4	100%	699	791
HTOJL95	806212	472	blastx.2	ORFI CODES FOR A 40 KDA PRODUCT.	sp Q15605 Q15605	63% 86% 57%	751 192 876	161
HTOJL95	762851	473	blastx.2	L1 ELEMENT L1.24 P40.	sp 000373 000373	71%	209	248

85	609	1308	1664	1444	1444	627	803	881		1696		314	391	185	128	116	1151	906	486	514	259		947	256	285	1681	1557	1469	1128	1216	19	241
279	683	553	1098	467	806	448	069	9		92		9	278	54	54	78	912	856	100	437	137		216	65	256	1854	1688	75	601	1040	∞	80
63%	32%	94%	%09	36%	36%	%98	75%	%66		100%		%86	73%	36%	48%	53%	25%	28%	78%	296	103.3		%68	%06	%06	63%	26%	%99	35%	100%	100%	32%
		sp Q9NW00 Q9NW00				sp Q9WUW2 Q9WUW2		sp AAG30222 AAG30222		sp P78371 TCPB_HUMA		emb CAB66746.1					sp Q9N083 Q9N083		dollar de la companya del companya della companya della companya de la companya de la companya de la companya della companya d		PF00129		pir 172752 172752			sp Q9N083 Q9N083		pir T30808 T30808	sp Q9V441 Q9V441	emb CAB66829.1		
		CDNA FL110404 FIS, CLONE	NT2RM4000486.			VESICLE ASSOCIATED	MEMBRANE PROTEIN 2B.	RNA polymerase III	transcription initiation factor BRFU.	T-COMPLEX PROTEIN 1, BETA SUBUNIT (TCP-1-	BETA) (CCT-BETA).	(AL136812) hypothetical	protein [Homo sapiens]				UNNAMED PORTEIN	PRODUCT.	HSPC171.		PFAM: Class I	Histocompatibility antigen, domains alpha 1 and 2	HLA-B*5501 - human			UNNAMED PORTEIN	PRODUCT.	hypothetical protein Sand - Fugu rubripes	BG:DS01219.1 PROTEIN.	(AL136895) hypothetical	protein [Homo sapiens]	
		blastx.2				blastx.2		blastx.2		blastx.2		blastx.2					blastx.2		blastx.2		HMMER	2.1.1	blastx.2			blastx.2		blastx.2	blastx.2	blastx.2		
		474				475		476		477		478					479		482		483					487		490	491	492		
		840596				637720		853401		840950		702027					561680		801935		844258					853410		834881	801938	844446		
		HTPDU17				HTSFJ32		HTTCB60		HTTEE41		HTTEZ02					HTWEH94		HTXDC38		HTXDC77					HTXFA72		HTXMZ07	HUFCL31	HUKBT67		

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sp BAB13989 BAB13989	pir S47481 S47481	gb AAG50014.1 AF32218	4_1		pir S34428 UQHUR	dbj BAA97098.1																						-					-	
CDNA FLJ12155 fis, clone MAMMA1000472.	tex261 protein - mouse	(AF322184) caspase	recruitment domain protein 8	[Homo sapiens]	ubiquitin / ribosomal protein CEP52 - human	(AP002460)	gene_id:F1D9.26~unknown	protein [Arabidopsis thaliana]																										
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270896	894699	792637			684975	762858																												
HUKDY82	HUSCJ14	HUSGL67			HUSGU40	HUSIR18																												

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[123] Table 2 further characterizes certain encoded polypeptides of the invention, by providing the results of comparisons to protein and protein family databases. The first column provides a unique clone identifier, "Clone ID NO:", corresponding to a cDNA clone disclosed in Table 1A and/or Table 1B. The second column provides the unique contig identifier, "Contig ID:" which allows correlation with the information in Table 1B. The third column provides the sequence identifier, "SEQ ID NO:", for the contig polynucleotide sequences. The fourth column provides the analysis method by which the homology/identity disclosed in the Table was determined. The fifth column provides a description of the PFAM/NR hit identified by each analysis. Column six provides the accession number of the PFAM/NR hit disclosed in the fifth column. Column seven, score/percent identity, provides a quality score or the percent identity, of the hit disclosed in column five. Comparisons were made between polypeptides encoded by polynucleotides of the invention and a non-redundant protein database (herein referred to as "NR"), or a database of protein families (herein referred to as "PFAM"), as described below.

[124] The NR database, which comprises the NBRF PIR database, the NCBI GenPept database, and the SIB SwissProt and TrEMBL databases, was made non-redundant using the computer program nrdb2 (Warren Gish, Washington University in Saint Louis). Each of the polynucleotides shown in Table 1B, column 3 (e.g., SEQ ID NO:X or the 'Query' sequence) was used to search against the NR database. The computer program BLASTX was used to compare a 6-frame translation of the Query sequence to the NR database (for information about the BLASTX algorithm please see Altshul et al., J. Mol. Biol. 215:403-410 (1990), and Gish and States, Nat. Genet. 3:266-272 (1993). A description of the sequence that is most similar to the Query sequence (the highest scoring 'Subject') is shown in column five of Table 2 and the database accession number for that sequence is provided in column six. The highest scoring 'Subject' is reported in Table 2 if (a) the estimated probability that the match occurred by chance alone is less than 1.0e-07, and (b) the match was not to a known repetitive element. BLASTX returns alignments of short polypeptide segments of the Query and Subject sequences which share a high degree of similarity; these segments are known as High-Scoring Segment Pairs or HSPs. Table 2 reports the degree of similarity between the Query and the Subject for each HSP as a percent identity in Column 7. The percent identity is determined by dividing the number of exact matches between the two aligned sequences in the HSP, dividing by the number of Query amino acids in the HSP and multiplying by 100. The polynucleotides of SEQ ID

NO:X which encode the polypeptide sequence that generates an HSP are delineated by columns 8 and 9 of Table 2.

[125] The PFAM database, PFAM version 2.1, (Sonnhammer, Nucl. Acids Res., 26:320-322, 1998))consists of a series of multiple sequence alignments; one alignment for each protein family. Each multiple sequence alignment is converted into a probability model called a Hidden Markov Model, or HMM, that represents the position-specific variation among the sequences that make up the multiple sequence alignment (see, e.g., Durbin, et al., Biological sequence analysis: probabilistic models of proteins and nucleic acids, Cambridge University Press, 1998 for the theory of HMMs). HMMER version 1.8 (Sean Eddy, Washington University in Saint Louis) was used to compare the predicted protein sequence for each Query sequence (SEQ ID NO:Y in Table 1B) to each of the HMMs derived from PFAM version 2.1. A HMM derived from PFAM version 2.1 was said to be a significant match to a polypeptide of the invention if the score returned by HMMER 1.8 was greater than 0.8 times the HMMER 1.8 score obtained with the most distantly related known member of that protein family. The description of the PFAM family which shares a significant match with a polypeptide of the invention is listed in column 5 of Table 2, and the database accession number of the PFAM hit is provided in column 6. Column 7 provides the score returned by HMMER version 1.8 for the alignment. Columns 8 and 9 delineate the polynucleotides of SEQ ID NO:X which encode the polypeptide sequence which show a significant match to a PFAM protein family.

[126] As mentioned, columns 8 and 9 in Table 2, "NT From" and "NT To", delineate the polynucleotides of "SEQ ID NO:X" that encode a polypeptide having a significant match to the PFAM/NR database as disclosed in the fifth column. In one embodiment, the invention provides a protein comprising, or alternatively consisting of, a polypeptide encoded by the polynucleotides of SEQ ID NO:X delineated in columns 8 and 9 of Table 2. Also provided are polynucleotides encoding such proteins, and the complementary strand thereto.

[127] The nucleotide sequence SEQ ID NO:X and the translated SEQ ID NO:Y are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, the nucleotide sequences of SEQ ID NO:X are useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in Clone ID NO:Z. These probes will also hybridize to nucleic acid molecules in biological samples, thereby

enabling immediate applications in chromosome mapping, linkage analysis, tissue identification and/or typing, and a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used to generate antibodies which bind specifically to these polypeptides, or fragments thereof, and/or to the polypeptides encoded by the cDNA clones identified in, for example, Table 1A and/or 1B.

[128] Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

[129] Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X, and a predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing cDNA Clone ID NO:Z (e.g., as set forth in columns 2 and 3 of Table 1A and/or as set forth, for example, in Table 1B, 6, and 7). The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. Further, techniques known in the art can be used to verify the nucleotide sequences of SEQ ID NO:X.

[130] The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

RACE Protocol For Recovery of Full-Length Genes

[131] Partial cDNA clones can be made full-length by utilizing the rapid amplification of cDNA ends (RACE) procedure described in Frohman, M.A., et al., Proc. Nat'l. Acad. Sci. USA, 85:8998-9002 (1988). A cDNA clone missing either the 5' or 3' end can be reconstructed to include the absent base pairs extending to the translational start or stop

codon, respectively. In some cases, cDNAs are missing the start codon of translation, The following briefly describes a modification of this original 5' RACE therefor. procedure. Poly A+ or total RNA is reverse transcribed with Superscript II (Gibco/BRL) and an antisense or complementary primer specific to the cDNA sequence. The primer is removed from the reaction with a Microcon Concentrator (Amicon). The first-strand cDNA is then tailed with dATP and terminal deoxynucleotide transferase (Gibco/BRL). Thus, an anchor sequence is produced which is needed for PCR amplification. The second strand is synthesized from the dA-tail in PCR buffer, Taq DNA polymerase (Perkin-Elmer Cetus), an oligo-dT primer containing three adjacent restriction sites (XhoI, SalI and ClaI) at the 5' end and a primer containing just these restriction sites. This double-stranded cDNA is PCR amplified for 40 cycles with the same primers as well as a nested cDNAspecific antisense primer. The PCR products are size-separated on an ethidium bromideagarose gel and the region of gel containing cDNA products the predicted size of missing protein-coding DNA is removed. cDNA is purified from the agarose with the Magic PCR Prep kit (Promega), restriction digested with XhoI or SalI, and ligated to a plasmid such as pBluescript SKII (Stratagene) at XhoI and EcoRV sites. This DNA is transformed into bacteria and the plasmid clones sequenced to identify the correct protein-coding inserts. Correct 5' ends are confirmed by comparing this sequence with the putatively identified homologue and overlap with the partial cDNA clone. Similar methods known in the art and/or commercial kits are used to amplify and recover 3' ends.

[132] Several quality-controlled kits are commercially available for purchase. Similar reagents and methods to those above are supplied in kit form from Gibco/BRL for both 5' and 3' RACE for recovery of full length genes. A second kit is available from Clontech which is a modification of a related technique, SLIC (single-stranded ligation to single-stranded cDNA), developed by Dumas et al., Nucleic Acids Res., 19:5227-32 (1991). The major differences in procedure are that the RNA is alkaline hydrolyzed after reverse transcription and RNA ligase is used to join a restriction site-containing anchor primer to the first-strand cDNA. This obviates the necessity for the dA-tailing reaction which results in a polyT stretch that is difficult to sequence past.

[133] An alternative to generating 5' or 3' cDNA from RNA is to use cDNA library double-stranded DNA. An asymmetric PCR-amplified antisense cDNA strand is synthesized with an antisense cDNA-specific primer and a plasmid-anchored primer. These primers are removed and a symmetric PCR reaction is performed with a nested cDNA-specific antisense primer and the plasmid-anchored primer.

RNA Ligase Protocol For Generating The 5' or 3' End Sequences To Obtain Full Length Genes

[134] Once a gene of interest is identified, several methods are available for the identification of the 5' or 3' portions of the gene which may not be present in the original cDNA plasmid. These methods include, but are not limited to, filter probing, clone enrichment using specific probes and protocols similar and identical to 5' and 3' RACE. While the full length gene may be present in the library and can be identified by probing, a useful method for generating the 5' or 3' end is to use the existing sequence information from the original cDNA to generate the missing information. A method similar to 5' RACE is available for generating the missing 5' end of a desired full-length gene. (This method was published by Fromont-Racine et al., Nucleic Acids Res., 21(7):1683-1684 (1993)). Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcript and a primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest, is used to PCR amplify the 5' portion of the desired full length gene which may then be sequenced and used to generate the full length gene. This method starts with total RNA isolated from the desired source, poly A RNA may be used but is not a prerequisite for this procedure. The RNA preparation may then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase if used is then inactivated and the RNA is treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase. This modified RNA preparation can then be used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction can then be used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the relevant gene.

[135] The present invention also relates to vectors or plasmids which include such DNA sequences, as well as the use of the DNA sequences. The material deposited with the ATCC (e.g., as described in columns 2 and 3 of Table 1A, and/or as set forth in Table 1B,

Table 6, or Table 7) is a mixture of cDNA clones derived from a variety of human tissue and cloned in either a plasmid vector or a phage vector, as described, for example, in Table 1A and Table 7. These deposits are referred to as "the deposits" herein. The tissues from which some of the clones were derived are listed in Table 7, and the vector in which the corresponding cDNA is contained is also indicated in Table 7. The deposited material includes cDNA clones corresponding to SEQ ID NO:X described, for example, in Table 1A and/or 1B (Clone ID NO:Z). A clone which is isolatable from the ATCC Deposits by use of a sequence listed as SEQ ID NO:X, may include the entire coding region of a human gene or in other cases such clone may include a substantial portion of the coding region of a human gene. Furthermore, although the sequence listing may in some instances list only a portion of the DNA sequence in a clone included in the ATCC Deposits, it is well within the ability of one skilled in the art to sequence the DNA included in a clone contained in the ATCC Deposits by use of a sequence (or portion thereof) described in, for example Tables 1A and/or 1B or 2, by procedures hereinafter further described, and others apparent to those skilled in the art.

[136] Also provided in Table 1A and 7 is the name of the vector which contains the cDNA clone. Each vector is routinely used in the art. The following additional information is provided for convenience.

[137] Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128, 256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., *Nucleic Acids Res.* 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., *Nucleic Acids Res.* 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., *Strategies* 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Phagemid pBS may be excised from the Lambda Zap and Uni-Zap XR vectors, and phagemid pBK may be excised from the Zap Express vector. Both phagemids may be transformed into *E. coli* strain XL-1 Blue, also available from Stratagene.

[138] Vectors pSport1, pCMVSport 1.0, pCMVSport 2.0 and pCMVSport 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, also available from Life Technologies. See, for instance, Gruber, C. E., et al., *Focus 15:59-* (1993). Vector lafmid BA (Bento Soares, Columbia University, New York, NY) contains an ampicillin resistance gene and can be transformed into *E. coli*

strain XL-1 Blue. Vector pCR[®]2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, available from Life Technologies. See, for instance, Clark, J. M., *Nuc. Acids Res.* 16:9677-9686 (1988) and Mead, D. et al., *Bio/Technology* 9: (1991).

[139] The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, and/or the deposited clone (Clone ID NO:Z). The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

[140] Also provided in the present invention are allelic variants, orthologs, and/or species homologs. Procedures known in the art can be used to obtain full-length genes, allelic variants, splice variants, full-length coding portions, orthologs, and/or species homologs of genes corresponding to SEQ ID NO:X or the complement thereof, polypeptides encoded by genes corresponding to SEQ ID NO:X or the complement thereof, and/or the cDNA contained in Clone ID NO:Z, using information from the sequences disclosed herein or the clones deposited with the ATCC. For example, allelic variants and/or species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for allelic variants and/or the desired homologue.

[141] The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

[142] The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below). It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

[143] The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified using

techniques described herein or otherwise known in the art, such as, for example, by the one-step method described in Smith and Johnson, Gene 67:31-40 (1988). Polypeptides of the invention also can be purified from natural, synthetic or recombinant sources using techniques described herein or otherwise known in the art, such as, for example, antibodies of the invention raised against the polypeptides of the present invention in methods which are well known in the art.

[144] The present invention provides a polynucleotide comprising, or alternatively consisting of, the nucleic acid sequence of SEQ ID NO:X, and/or the cDNA sequence contained in Clone ID NO:Z. The present invention also provides a polypeptide comprising, or alternatively, consisting of, the polypeptide sequence of SEO ID NO:Y, a polypeptide encoded by SEQ ID NO:X or a complement thereof, a polypeptide encoded by the cDNA contained in Clone ID NO:Z, and/or the polypeptide sequence encoded by a nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1C. Polynucleotides encoding a polypeptide comprising, or alternatively consisting of the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X, a polypeptide encoded by the cDNA contained in Clone ID NO:Z, and/or a polypeptide sequence encoded by a nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1C are also encompassed by the invention. The present invention further encompasses a polynucleotide comprising, or alternatively consisting of, the complement of the nucleic acid sequence of SEQ ID NO:X, a nucleic acid sequence encoding a polypeptide encoded by the complement of the nucleic acid sequence of SEQ ID NO:X, and/or the cDNA contained in Clone ID NO:Z.

[145] Moreover, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in Table 1C column 6, or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in Table 1C column 6, or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1C, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1C, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1C, column 6, and have a nucleic

acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1C, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

[146] Further, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1C which correspond to the same Clone ID NO:Z (see Table 1C, column 1), or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in column 6 of Table 1C which correspond to the same Clone ID NO:Z (see Table 1C, column 1), or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of. sequences delineated in column 6 of Table 1C which correspond to the same Clone ID NO:Z (see Table 1C, column 1) and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1C, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1C which correspond to the same Clone ID NO:Z (see Table 1C, column 1) and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). In additional embodiments, the abovedescribed polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1C which correspond to the same Clone ID NO:Z (see Table 1C, column 1) and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

[147] Further, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1C which correspond to the same contig sequence identifer SEQ ID NO:X (see Table 1C, column 2), or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in column 6 of Table 1C which correspond to the same contig sequence identifer SEQ ID NO:X (see Table 1C, column 2), or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1C which correspond to the same contig sequence identifer SEQ ID NO:X (see Table 1C, column 2) and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1C, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1C which correspond to the same contig sequence identifer SEQ ID NO:X (see Table 1C, column 2) and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1C which correspond to the same contig sequence identifer SEQ ID NO:X (see Table 1C, column 2) and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (See Table 1C, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

[148] Moreover, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in the same row of Table 1C column 6, or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in the same row of Table 1C column 6, or any combination thereof. In preferred embodiments, the polynucleotides of

the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in the same row of Table 1C column 6, wherein sequentially delineated sequences in the table (i.e. corresponding to those exons located closest to each other) are directly contiguous in a 5' to 3' orientation. In further embodiments, above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1C, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1C, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1C, column 6, and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1C, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1C, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[149] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1C, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1C, column 2) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[150] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1C which correspond to the same Clone ID NO:Z (see Table 1C, column 1), and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A, 1B, or 1C) or fragments or variants thereof. In preferred embodiments, the delineated sequence(s) and polynucleotide sequence of SEQ ID NO:X correspond to the same Clone ID NO:Z. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[151] In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in the same row of column 6 of Table 1C, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A, 1B, or 1C) or fragments or variants thereof. In preferred embodiments, the delineated sequence(s) and polynucleotide sequence of SEQ ID NO:X correspond to the same row of column 6 of Table 1C. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[152] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of the sequence of SEQ ID NO:X are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[153] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X are directly contiguous Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[154] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of the sequence of SEQ ID NO:X and the 5' 10 polynucleotides of the sequence of one of the

sequences delineated in column 6 of Table 1C are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[155] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X and the 5' 10 polynucleotides of the sequence of one of the sequences delineated in column 6 of Table 1C are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides, are also encompassed by the invention.

[156] In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of another sequence in column 6 are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[157] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of

another sequence in column 6 corresponding to the same Clone ID NO:Z (see Table 1C, column 1) are directly contiguous. Nucleic acids which hybridize to the complement of these 20 lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[158] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one sequence in column 6 corresponding to the same contig sequence identifer SEQ ID NO:X (see Table 1C, column 2) are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[159] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C and the 5' 10 polynucleotides of another sequence in column 6 corresponding to the same row are directly contiguous. In preferred embodiments, the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1C is directly contiguous with the 5' 10 polynucleotides of the next sequential exon delineated in Table 1C, column 6. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[160] Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. Accordingly, for each contig sequence (SEQ ID NO:X) listed in the fifth column of Table 1A and/or the fourth column of Table 1B, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 and the final nucleotide minus 15 of SEQ ID NO:X, b is an integer of 15 to the final nucleotide of SEQ ID NO:X, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:X, and where b is greater than or equal to a + 14. More specifically, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a and b are integers as defined in columns 4 and 5, respectively, of Table 3. In specific embodiments, the polynucleotides of the invention do not consist of at least one, two, three, four, five, ten, or more of the specific polynucleotide sequences referenced by the Genbank Accession No. as disclosed in column 6 of Table 3 (including for example, published sequence in connection with a particular BAC clone). In further embodiments, preferably excluded from the invention are the specific polynucleotide sequence(s) contained in the clones corresponding to at least one, two, three, four, five, ten, or more of the available material having the accession numbers identified in the sixth column of this Table (including for example, the actual sequence contained in an identified BAC clone). In no way is this listing meant to encompass all of the sequences which may be excluded by the general formula, it is just a representative example. All references available through these accessions are hereby incorporated by reference in their entirety.

TABLE 3

Clone ID	SEQ ID NO:	Contig ID:	EST Dis	sclaimer Range of b	Accession #'s
H6BSF56	11	762968	1 - 591	15 - 605	AW958287, BF027085, AV650800, AV650218, BF689895, BE409727, BE871017, BE278963, BF975253, AA449214, AA150070, BF247445, AA310756, BF337859, AA425098, BE746295, BE732859, BE742068, R48107, BF129114, AA393871, AI707816, AI523073, AW002940, BE672910, BF764476, AW827130, AA468022, AA493695, AW857950, AW275510, AW857971,

AI223604, AI254279, BE179557, BG059450, AW963750, AI445674, AW979031. AV703942, AV762535, AI687343, BG249643, AA769402, AW827120, AA484373, AI345157, AV739452, AW168618, AW504900, AA467876, BF887977, AV710066, AV763354, AV762098, AI744826, BF964993, AA279421, AW302903, AW872575, AI700109, BF437493, AV764329, BE253048, AW270343, AL046205, BE782280, BF677892, AV759437, AV734583, AV760777, AV760486, BF965007, BE907585. AV764578, AW131249, BE297262, BF347740, BF337291, BF679274, AW193265. AI247199, BF347791, AV764307, AV763183, AW235497, AA747070, BF760796, AW872676, AI004704, AW002350, AI270117, AI311927, BF871137, BE883107, AL043009, AI754658, AI250083, AV760258, AW069769, AI370094, AL119691. AW063143, AI270559, AA372481. AV760937, AL119713, AW857949, BF742624, AA720702, BE736829, BF681649, AI953275, AA490183, AF330238. AW970871, AU145314, BF977376, AL138265, AV759172, AV761106, AV735614, AW953071, AA019312, AA584167, AV728425, AU121243, AV763847, AL038799, AV733830, BF965154, BG026806, AI133164, AA523841, AV763540, AV762050, AI470646, AI284640, AI307022, AA635739, AI350211, BE350772, AI691091, AI251082, AI370074, BF936005, AI305766, AI732378, AI860013, AV744393, AW974109, AW500125, AV760378, AV734666, AV764241, AL037683, AL038705, AA683238, BG023888, AK025830, AF151821, AB015724, AC004760, AC005089, AC005988, AL049766, AC005257, AL117377, AL109936, AC009311, AC007383, AC018637, AL161445, AL034545, L78833, AC005250, AC006511, AL136223, Z95115, AC006999, AC005606, AL022322, AC007011, AC007279, AC007428, AC002476, AL049795, AC016576, Z98051, AC011508, AL021393, AC006285, AC005923, AL137839, AC003101, AL121934, AC020893, AC004638, AP001753, AC007620, AC010524, AF215937, AL117332, AL022163, AC008482, AC006077, AC022432, AC011559, AL121586, AC004849, AC019215, AC005071, AL022238, AL034423, AC006275, AL354720, AC002314, Z82198, AL137780, AC005694, AC010422, AF252830, AC004686, AL121751, AC004814, AC024084, AC005280, AC007192, AC002430, AL157938, AP001680, AL031777, AL353748, AL021807, AL136131, AC002395, AL136969, AL020997,

					AC005258, AC018633, AL118501,
					AC018720, AL135818, AC004008,
					AC006111, AL035462, AC002470,
					AC016025, AC007384, AC018712,
					AL136308, AL035667, AC004876,
					AC005020, AC002425, AL109823,
					AL034420, AC007216, AC004650,
			1		AC007225, AL078611, AF001549, Z69706,
	1	ļ			AP001725, AL049544, AL121892, U63630,
					AL499629, AC010271, AL008725, AL021939,
					AL445687, AF254822, AC002531, AL121601,
					AL022237, AC004388, AC011310,
					AL031311, AC005527, AL050349, Z68162,
					AL121903, AC007546, AC020917,
			İ]	AL139186, Z93241, AC015853, AC020934,
					AF117829, Z82190, AC022150, AL360227,
					AL157931, AC004980, AL121897,
					AC004622, Z83844, AC005288, AX039602,
			•		AP001687, AL031286, AC022027, AL117258,
					AC005821, AC004899, AL391839,
1					AL356414, AP001746, Z97196, AL109921,
		1		•	AL031662, AC004598, AC015555, Z83845,
·					AC008372, AL080242, AL137061,
	ŀ				AC012309, AC004659, AC004755, AJ229043,
					AL137853, AC008770, AF228703, AC011477,
<u> </u>					AC020916, AC008521, AL021578, M63796,
					AL009181, AC006312, AC024561,
			:		AC005488, AC005274, AC006130,
	ł				AP001721, AC021752, AL008712, AC004534,
					AC023105, AC006277, AL133282,
					AC005529, U63312, AC016395, AC005484,
					AC005531, AL033520, AC001231,
]	AC004894, AL136137, AC073976, Z98742,
					AL035079, AF047825, AC002301, Z98752,
				1	AC008976, AL359695, AL035424,
					AC018644, U95742, Z99716, AL031650,
					AC010609, AC013436, AC011531,
					AC006501, AC006017, Z98750, AL133289,
					AL135901, AF317635, AL009183, AL138976,
					AL023284, AP000962, AF042090, AC000066,
					AC009481, AC022517, AC007450,
					AC005600, AL121952, AC007262,
					AL117382, AL365335, AC008886,
					AC020906, AF243527, AL049537, AC008088,
					AP000501, AC006451, AL353807, AP000555,
					AC008403, AC009277, AF108083,
			,		AC005081, AL078590, AC005778, and
]			AL450226.
H6EDM64	12	841331	1 - 2596	15 - 2610	AL529288, AL514648, AL523579, AL523918,
		_			AL530571, AL528848, AL523917, AL523578,
					BE795355, BE614208, AL529287, BE797988,
					BE747962, BE798201, AL530750, BF689293,
					BE884814, BF508994, BE798313, BE613450,
					BE787266, AW131835, AL530749,
					BG248495, BE386285, BF526775, BE873469,
					BE299650, AL042569, BE621187, BG168950,
					AW410458, BE883794, BE869375,
					BF348689, AW239351, BE737181,
					BE734276, BF309636, BF129214, BG180549,
					AW410610, AW601905, BE621858,
·	·	·	L	L	1

				1	AA689552, BF310547, AW960649,
					BF953086, AL045821, BE882424, BF724804,
					BE019151, AW246108, BG179779,
					AW374338, AW675186, BE279317,
			<u>}</u>		BG011956, AI475847, AI394166, AI142042,
			·		AW068652, AI539419, AI970048, AI792316,
		1		1	AA536006, AW272491, BG012645,
1					AI827847, BG254459, AI673493, AW007399,
1					AI719374, AA994188, BG176564, AI707847,
					AW104963, AI220974, AA022523, BF807054,
					BG012634, BF803094, N24911, AW665019,
					AI458806, AA689495, AA480131, AI808412,
					N41812, W17347, BE772562, BG012642,
		1			BF807055, BE772573, BG011957, BG012641,
					AL514647, F22287, AI160580, AI149344,
			•		BE772556, AI870582, BE772568, AW801577,
					BG176616, AW801325, AW068651,
		l			AI197831, BE265961, AA483525, BE772566,
					BE772574, BE693737, AA687509, BE839398,
					BF799200, AA687451, AI201450, BF896481,
]		BE772569, BE244158, BE772576, BE826728,
	į.			l	
	İ				AI452812, BE772561, AA317941, AA308425,
					AA745895, AW751437, BG256219,
1	ł	1			AA782657, BF373198, AA364848,
					AL039960, AA405870, AW963550,
		l			BE300303, N78953, AA112404, BE826586,
					AI061434, AI143698, AW087863, AI382254,
	1	1			AW731818, BE788591, AW304748,
		·			AI589259, AA357514, BF663656, AW673017,
					AW664622, AA524482, AW246627,
		1			BE831243, BE831271, BG055766, AI749023,
	1				AA380438, BF746714, BE839346,
	1				AW084279, AA113160, BF529848, AI160508,
					BF764174, BF752908, AA053148,
					AW842671, F32117, AI190107, BF752929,
					BE547478, AA977756, AA360528,
	,				AA022454, BF808843, BF813892, AI917965,
					BG011699, BG012316, BF373193, BG122581,
					AA622680, BF688484, BE772558, AA053706,
					AA733114, BG012318, AW880294,
					AA482098, BE256450, BE831281, BF765811,
					BF803085, BE243388, AA774840, AA576098,
					BE831236, BE772816, AF024631, AX011724,
					AX015345, AF096303, U73627, AF061779,
					AC004923, AF238378, and AC000385.
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HCEDR26	80	771144	1 - 1405	15 - 1419	AW809560, BF822291, AW805745, T06675, T41328, AW809450, BF884442, BF773357, BF738231, BE163588, BF998055, H00095, BF900030, AA346118, AA644090, BF725844, BF725688, AI919265, AI801505, AW103406, AW855803, BF673854, AA833896,

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